APPENDIX C

Dr. W. Marcus Cooke
Curriculum Vitae

Resume

William Marcus Cooke, Ph.D.

Experience Summary

Dr. Cooke has 24 years experience managing laboratories that conduct genotoxics characterization programs for industrial and governmental clients. Under Dr. Cooke's direction these laboratories developed regulatory reports for clients, have given public testimony before national hearings, presented research results at technical symposia, and published extensively on characterization of complex materials. He has developed general environmental analysis methods for the U.S. Environmental Protection Agency (EPA), and managed method validation programs for EPA.

Dr. Cooke has published extensively on complex families of chemicals such as polynuclear aromatic hydrocarbons (PAH), polychlorinated biphenyls (PCB), polychlorinated dibenzo-p-dioxins (PCDD or 'dioxin'), and polychlorinated dibenzofurans (PCDF 'furan'). His publications include seven books, numerous technical articles and reports.

Dr. Cooke has directed three laboratories that conducted high resolution mass spectrometric analysis of PAH, PCDD, PCDF and PCB. He has conducted investigations of these species in a number of matrices including studies of most combustion types. This experience has allowed Dr. Cooke to elucidate compositional patterns in these compounds.

Dr. Cooke has managed laboratories that conducted sponsored programs to develop analytical methods for chemical species including pesticides, wood preservatives, pesticide decay products and metabolites. Dr. Cooke has conducted analytical and development programs under Good Laboratory Practices (GLP), and has presented data to the Food and Drug Administration.

Dr. Cooke directs American Chemical Society, environmental training programs which include a series of two day courses that are offered throughout the United States. One course, "Methods of Analysis for Water and Waste Using U.S. EPA Methods" has been taught to over 3,000 U.S. laboratory professionals and addresses analysis and data interpretation for complex organics including PCP, PCDD, PCDF, PCB and PAH, and elemental species including metal and speciated metal constituents.

Dr. Cooke has held teaching positions at the University of North Carolina (Charlotte), the Free University of Brussels, the University of Puerto Rico (Rió Piedras and Humacao), and Beijing Polytechnic University. Dr. Cooke is fluent in French, and communicates in several languages. Dr. Cooke has managed laboratories and program offices in Australia, Belgium, Brazil, China(PRC), England, Finland, Germany, Japan, Mexico, Russia, and South Africa.

Dr. Cooke has participated in numerous risk assessment and identification programs. He presented the 1996 Keynote Address on Risk Assessment at the U.S./Korea National Seminar on Risk Management and Public Policy in Seoul. Dr. Cooke was co-recipient of the U.S. EPA's National Research Award in 1989 for a joint U.S.-China (PRC) study on carcinogenicity of polynuclear aromatic compounds in coal smoke.

Employment History

General Manager, CCI, 1996-present.
Dr. Cooke manages a scientific services group that conducts contract studies in pollutant testing, removal and remediation. CCI is involved in laboratory measurements, risk assessment, and regulatory required programs in Asia, Europe, Latin America, and North America.

President, International Division, Triangle Laboratories (TL), 1994 - 1996.
Dr. Cooke was responsible for international business activities at Triangle Laboratories. Triangle Laboratories provides laboratory services at eight international facilities located in: Australia, Brazil , England, Germany, Japan, Mexico, Russia, and South Africa.

Distinguished Technical Associate, International Technology Corporation (ITC), 1989 - 1994.
As Distinguished Technical Associate (the senior science officer for IT Corporation's Analytical Services Division), Dr. Cooke was responsible for technical liaison and program management on large environmental studies, including commercial and Federal remediation of operating and abandoned waste sites. IT operated the largest commercial chemical analysis service in the U.S. IT's laboratory system had 11 laboratories with 900 chemists employed. Dr. Cooke was the senior chemist responsible for the IT laboratories.

Program Manager for Chemistry, Battelle Memorial Institute, Columbus, Ohio, 1980 - 1989.
Directed a research group studying organic compounds (scientists and technicians), and managed programs in environmental chemistry. The Program Manager position at Battelle involved line management, bidding, directing contract research using in-house staff and subcontractors, and supervising timely reporting. Key programs included supervision of four Federal method validation contracts, management of several large industrial contracts to study commercial products, FDA submittal support, pesticide and agrochemical characterization programs, and direction of major combustion engineering studies.

Laboratory Director, Mead CompuChem Laboratories, Research Triangle Park, NC, 1978 - 1980.
Started an analytical services division for Mead Paper company. Principal author of a plan for the first commercial analytical service business in the United States . While at Mead

instituted the first traveler system to track samples through all stages of processing, developed one of the first organized quality assurance programs in environmental testing, and institutionalized strict codes of professional conduct for laboratory staff.

Associate Professor of Chemistry, University of North Carolina, Charlotte, NC, 1972 - 1978. Directed a research program in environmental analytical chemistry and taught graduate and undergraduate chemistry courses. This was a tenured position with research supported mainly by the National Science Foundation and the U.S. Environmental Protection Agency.

Employment History (Continued)

Chemist, U.S.- Environmental Protection Agency, Research Triangle Park, NC, 1973 - 1977. Worked for the U.S. Environmental Protection Agency from 1972 to 1979 as a chemist at the National Environmental Research Center, Research Triangle Park, North Carolina, performing methods development studies for hazardous air pollutants. This appointment involved developing methods for the analysis of organic and inorganic gaseous pollutants in mobile sources, ambient air, and direct source measurements. Dr. Cooke developed techniques for measuring atmospheric oxidants, and environmental genotoxicants.

Education

Bachelor of Science, Mathematics and French (1965), Appalachian State Univ., Boone, NC.
Master of Science, Chemistry (1969), Appalachian State Univ., Boone, NC.
Doctor of Philosophy, Chemistry (1972), The Virginia Polytechnic Institute and State University, Blacksburg, VA.

Awards and Recognition

Dr. Cooke is the author or editor of seven books on environmental organic chemistry, several technical papers, and has given numerous technical presentations on environmental chemistry. His awards include:

[1] U.S.-Environmental Protection Agency's Scientific and Technological Achievement Award (1987 Corecipient), for studies on the relationship of cancer with organic pollutants in smoke.
[2] Chairman, International Symposium on Polynuclear Aromatic Hydrocarbons, 1980 - 1991.

[3] Senior Fulbright Fellow, Vrije Universiteit Brussel (Free University of Brussels), 1975-1976.
[4] Visiting Professor of Chemistry, University of Puerto Rico, 1986.
[5] Lecturer, Finnish Power Authority (1986-1988).
[6] Moderator, Environmental Education Program, American Chemical Society, 1979 to the present.
[7] Adjunct Professor of Chemistry, U.S. Environmental Protection Agency, since 1973.

Publications

Recent Publications:

Cooke, M., and Sellers R., "New FDA Surveys on Dioxin in Feed", Vol. 51, (3), March , 2000, pp. 19-21.

Cooke, M., Clark, G.C., Goeyens L., and and W. Baeyens, "Bioanalytical Dioxin Tests, New, Accurate, and Affordable, an Alternative to Instrumental Methods", Today's Chemist at Work, July 2000, In Press.

Books:

Cooke, M., Loening, K., and Merritt, J., Polynuclear Aromatic Hydrocarbons: Measurements, Means and Metabolism, Battelle Press (Columbus, Ohio), 1990, 1220 pp.

Cooke, M., and Dennis, A., Polynuclear Aromatic Hydrocarbons: A Decade of Progress, Battelle Press (Columbus, Ohio), 1988, 960 pp.

Cooke, M., and Dennis, A., Polynuclear Aromatic Hydrocarbons: Chemistry, Characterization and Carcinogenesis, Battelle Press (Columbus, Ohio), 1986, 1088 pp.

Cooke, M., and Dennis, A., Polynuclear Aromatic Hydrocarbons: Mechanisms, Methods and Metabolism, Battelle Press (Columbus, Ohio) 1984, 1464 pp.

Cooke, M., and Dennis, A., Polynuclear Aromatic Hydrocarbons: Formation, Metabolism and Measurement, Battelle Press (Columbus, Ohio), 1983, 1344 pp.

Rondia, D., Cooke, M., and Haroz, R.K., Mobile Source Emissions Including Polycyclic Organic Species, D. Reidel Publishing Company (Dordrecht, Holland), 1982, 387 pp.

Cooke, M., and Dennis, A., Polynuclear Aromatic Hydrocarbons: Physical and Biological Chemistry, Battelle Press (Columbus, Ohio), 1981, 800 pp.

In addition Dr. Cooke is the author or co-author of numerous refereed articles, reports, book chapters, and technical presentations. Dr. Cooke has given invited lectures in 12 countries..

Contact Information

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APPENDIX D

Dr. Walter W. Piegorsch
Curriculum Vitae

June, 2002

Walter W. Piegorsch

Education

1979 B.A. (Mathematics), *magna cum laude,* Colgate University, Hamilton, NY
1982 M.S. (Statistics), Cornell University, Ithaca, NY
1984 Ph.D. (Statistics), Cornell University, Ithaca, NY

Experience

1979 - 1983	Visiting Administrator/Programming Director, Washington Workshops Congressional Seminar, Washington, DC
1979 - 1984	Teaching Assistant, Biometrics Unit and School of Operations Research, Cornell University, Ithaca, NY
1984 - 1993	Mathematical Statistician, Statistics and Biomathematics Branch, National Institute of Environmental Health Sciences, Research Triangle Park, NC
1988 - 1993	Adjunct Associate Professor of Statistics, North Carolina State University, Raleigh, NC
1993 - 1997	Adjunct Associate Professor of Statistics and Biostatistics, University of North Carolina, Chapel Hill, NC
1993 - 1996	Associate Professor of Statistics, University of South Carolina, Columbia, SC
1994 - 1999	Adjunct Associate Professor of Epidemiology and Biostatistics, University of South Carolina, Columbia, SC
1998 - 2002	Adjunct Professor of Biostatistics, University of North Carolina, Chapel Hill, NC
1999 - 2002	Adjunct Professor of Epidemiology and Biostatistics, University of South Carolina, Columbia, SC
1995 - date	Associated Faculty, School of the Environment, University of South Carolina, Columbia, SC
1996 - date	Professor of Statistics, University of South Carolina, Columbia, SC
1998 - date	Director of Undergraduate Studies, Department of Statistics, University of South Carolina, Columbia, SC

Honors

1976 - 1979	New York State Regents Scholar
1979	Elected to New York Eta Chapter, Phi Beta Kappa
1981	Outstanding Teaching Assistant in Statistics, College of Agriculture and Life Sciences, Cornell University
1982 - 1983	Cornell University Graduate School Fellow
1983	Charter member, New York Alpha Chapter, Mu Sigma Rho, The National Honor Society in Statistics
1988	National Institutes of Health Quality Performance Awards (also 1990, 1992, 1993)
1993	Distinguished Achievement Medal, American StatisticalAssociation Section on Statistics and the Environment
1995	Fellow, American Statistical Association

Honors (cont'd)

1995	Member (by election), International Statistical Institute
2000	Recipient, University of South Carolina Educational Foundation Research Award for Science, Mathematics, and Engineering

Professional Activities

Member, American Statistical Association, International Biometric Society, International Environmetric Society, Environmental Mutagenesis Society, International Statistical Institute.

Co-Editor-in-Chief, *Encyclopedia of Environmetrics*, John Wiley & Sons, Chichester, UK, 1999 - 2002.

Associate Editor

- *J. Amer. Statist. Assoc.*, Biopharmaceutical Special Section, 1987 - 1989. Theory & Methods Section, 1996 - 2005.
- *Environmetrics*, 1992 - date.
- *Environ. Ecol. Statist.*, 1994 - date.
- *Biometrics*, 1997 - 2005.

Co-Guest Editor, *Environmetrics* Special Issue on Environmental Biometry, December 1993.

Member, Editorial Board

- *Environmental Health Perspectives* (Editorial Review Board), 1993 - 1996.
- *Environmental and Molecular Mutagenesis*, 1994 - date.
- *Mutation Research*, 1994 - date.

Member, Board of Scientific Counselors, U.S. National Toxicology Program, 2000 - 2004.

External Reviewer, Department of Mathematics and Statistics, Miami University, Oxford, OH, 2001.

Chairman, Review Panel

- U.S. National Institutes of Health Special Emphasis Panel ZES1 ZEH-D (CS), 2001.

Member, Review Panel

- U.S. Environmental Protection Agency Innovative Research Funding Program, 1993.
- U.S. National Science Foundation/Conference Board of the Mathematical Sciences Regional Conferences Funding Program, 1997, 1998.
- U.S. Environmental Protection Agency/National Science Foundation Environmental Statistics Funding Program, 1998, 1999.
- International Coordinating Committee on the Validation of Alternative Methods Endocrine Disruptor Expert Panel, 2002.

Committee Chair

- International Conference on Environmental Biometrics Organizing Committee (Co-Chairman), Sydney, Australia, December 1992.
- Joint Statistical Meetings Program Committee, Toronto, ON, August 1994.
- American Statistical Association Section on Statistics and the Environment Strategic Planning Committee, 1994 - 1995.
- International Biometric Society Eastern North American Region Task Force on Internet Services, 1996.

Professional Activities (cont'd)

- International Program Committee, International Conference on Statistical Challenges in Environmental Health Problems, Fukuoka City, Japan, August 2001.

Committee Member

- American Statistical Association Committee on Meetings, 1993 - 1995.
- International Statistical Institute Satellite Conference on Chemometrics and Environmetrics Organizing Committee, Bologna, Italy, August 1993.
- International Environmetric Society Meeting Scientific Committee, Burlington, ON, August 1994.
- Environmental Mutagenesis Society Working Group on Transgenic Mouse Assays, 1994 - 1995.
- American Statistical Association Committee on Committees, 1995 - 1996.
- American Statistical Association Section on Statistics and the Environment Nominations Committee, 1997.
- American Statistical Association Summer Research Conference in Statistics Organizing Committee, Navarre Beach, FL, June 1998.
- Joint Statistical Meetings Program Committee (ENAR Program Chair), Baltimore, MD, August 1999.
- International Biometric Society Eastern North American Region Committee on Website Oversight, 1999 - 2001.
- Regional Committee (RECOM), International Biometric Society Eastern North American Region, 1999 - 2001.
- Journal Management Committee, *Journal of Agricultural, Biological, and Environmental Statistics*, 2000 - 2005.
- International Biometric Society Eastern North American Region Education Advisory Committee, 2001 - 2002.

Liaison Officer, Section on Statistics and the Environment, American Statistical Association, 1991 - 1992.

Secretary, International Biometric Society Eastern North American Region, 1995 - 1996.

Vice-Chair, American Statistical Association Council of Sections Governing Board, 1997 - 1999.

Council Member, International Biometric Society, 2002 - 2004.

Chair-elect, Section on Statistics and the Environment, American Statistical Association, 2003.

Dissertation adjudicator/examiner

- Nagarjuna University, Nagarjuna, India, 1990, 1993.
- Andhra University, Waltair, India, 1991.
- Sambalpur University, Sambalpur, India, 2000.

Textbook Reviewer/Software Reviewer

- John Wiley & Sons, 1994, 2000.
- W. H. Freeman & Co., 1994, 1999.
- Springer-Verlag, 1995.
- Arnold Publishers, 2000.

Sponsored Research

1982 - 1984 Student Investigator, Sigma Xi Research Awards (Cornell Chapter): Interval Estimation in Regression.

Sponsored Research (cont'd)

1987 - 1993	Principal Investigator, Public Health Service Intramural Research Project #Z01-ES-48001: Statistical analysis of data from genotoxicological experiments.
1996	Principal Investigator, University of South Carolina School of the Environment Research Award: Modeling dose response and statistical overdispersion in environmental toxicity assays.
1997 - 2003	Principal Investigator, Public Health Service Extramural Research Project #R01-CA-76031: Low-dose risk bounds via simultaneous confidence bands.
2000	Co-Principal Investigator, South Carolina Commission on Higher Education Research Initiative Grant #13010-G121: On the analysis and interpretation of biological sequence data. (P.I.: Austin L. Hughes.)
2001	Co-Investigator, Univ. of South Carolina Office of Research Grant #13080-A050: Environmental statistics. (P.I.: Don Edwards.)

Students Supervised

1. Slaton, Terra L. (M.S., Statistics): Modeling hierarchical beta parameters with overdispersed proportion data, May, 1995.
2. Richwine, Kelly A. (M.S., Statistics): Pairwise comparisons among multinomial proportions, May 1996.
3. Dickenson, Tammiee S. (M.S., Statistics): Inferences on the probability of response under the Heckman-Willis model for overdispersed proportion data, December 1996.
4. Beatty, Dena A. (M.S., Statistics): Statistical design considerations for toxicokinetic studies, May 1997.
5. Tu, Wanzhu (Ph.D., Statistics): Empirical Bayes analysis of count data, August 1997.
6. Rekowski, Angela M. (M.S., Statistics): Low-dose extrapolation of discrete toxicological data, May 1998.
7. Scritchfield, Kelly D. (M.S., Statistics): Asymmetric Bowden-type confidence bands for linear regression over intervals, May 1999.
8. Al-Saidy, Obaid M. (Ph.D., Statistics): Confidence bands for low-dose risk estimation with quantal response data, August 2001.
9. Pan, Wei (Ph.D., Statistics): One-sided confidence bands for low-dose risk estimation with nonquantal data, May 2002.
10. Simmons, Susan J. (Ph.D., Statistics): Hierarchical normal models for meta-analysis of mutagenic potency, (in progress).
11. Nitcheva, Daniela. (Ph.D., Statistics): Hierarchical regression models for meta-analysis of mutagenic potency, (in progress).

Publications

1. Piegorsch, W.W. The questions of fit in the Gregor Mendel controversy. *Communications in Statistics – Theory and Methods* 12, 2289-2304 (1983).

Publications (cont'd)

2. Piegorsch, W.W. Regularity conditions, asymptotics, and the exponential class. *Proceedings of the American Statistical Association, Section on Statistical Education,* 126-129 (1983).
3. Piegorsch, W.W. Has J.G. Mendel been "too accurate" in his experiments? The χ^2 test and its significance to genetic segregation. *Historia Mathematica* **10**, 99-100 (1983).
4. Piegorsch, W.W. Can we generate a bivariate Poisson distribution with a negative correlation? (Unsolved Problem) *American Mathematical Monthly* **91**, 562 (1984).
5. Piegorsch, W.W. and Casella, G. The existence of the first negative moment. *American Statistician* **39**, 60-62 (1985).
6. Piegorsch, W.W. Admissible and optimal confidence bands in simple linear regression. *Annals of Statistics* **13**, 801-810 (1985).
7. Piegorsch, W.W. Average width optimality for confidence bands in simple linear regression. *Journal of the American Statistical Association* **80**, 692-697 (1985).
8. Piegorsch, W.W. The Gregor Mendel Controversy: Early issues of goodness-of-fit and recent issues of genetic linkage. *History of Science* **24**, 173-182 (1986).
9. Piegorsch, W.W. Confidence bands for polynomial regression with fixed intercepts. *Technometrics* **28**, 241-246 (1986).
10. Piegorsch, W.W. and Gladen, B.C. A note on the use of prior interval information in constructing interval estimates on a gamma mean. *Technometrics* **28**, 269-273 (1986).
11. Piegorsch, W.W., Weinberg, C.R., and Haseman, J.K. Testing for simple independent action between two factors for dichotomous response data. *Biometrics* **42**, 413-419 (1986).
12. Piegorsch, W.W. and Weinberg, C.R. Testing for synergistic effects for simultaneous exposures with stratified dichotomous response. *Journal of Statistical Computation and Simulation* **26**, 1-19 (1986).
13. Rao, G.N, Piegorsch, W.W., and Haseman, J.K. Influence of body weight on the incidence of spontaneous tumors in rats and mice of long term studies. *American Journal of Clinical Nutrition* **45**, 252-260 (1987).
14. Piegorsch, W.W. Performance of likelihood-based interval estimates for two-parameter exponential samples subject to type I censoring. *Technometrics* **29**, 41-49 (1987).
15. Kitamura, H., Inayama, I., Ito, T., Yanaba, M., Piegorsch, W.W., and Kanisawa, M. Morphologic alteration of mouse Clara cells induced by glycerol: ultrastructural and morphometric studies. *Experimental Lung Research* **12**, 281-302 (1987).
16. Piegorsch, W.W. On confidence bands and set estimators in simple linear regression. *Statistics and Probability Letters* **5**, 409-413 (1987).
17. Piegorsch, W.W. Model robustness for simultaneous confidence bands. *Journal of the American Statistical Association* **82**, 879-885 (1987).
18. Piegorsch, W.W. Discretizing a normal prior for change point estimation in switching regressions. *Biometrical Journal* **29**, 777-782 (1987).

Publications (cont'd)

19. Piegorsch, W.W., Weinberg, C.R., and Margolin, B.H. Exploring simple independent action in multifactor tables of proportions. *Biometrics* **44**, 595-603 (1988).
20. Dunnick, J.K., Eustis, S.L., Piegorsch, W.W., and Miller, R.A. Respiratory tract lesions in F344/N rats and B6C3F$_1$ mice after exposure to 1,2-Epoxybutane. *Toxicology* **50**, 69-82 (1988).
21. Piegorsch, W.W. and Hoel, D.G. Exploring relationships between mutagenic and carcinogenic potencies. *Mutation Research* **196**, 161-175 (1988).
22. Piegorsch, W.W. and Casella, G. Confidence bands for logistic regression with restricted predictor variables. *Biometrics* **44**, 739-750 (1988).
23. Piegorsch, W.W. Quantification of toxic response and the development of the median effective dose (ED_{50}) – An historical perspective. *Toxicology and Industrial Health* **5**, 55-62 (1989).
24. Piegorsch, W.W. and Margolin, B.H. Quantitative methods for assessing a synergistic or potentiated genotoxic response. *Mutation Research* **216**, 1-8 (1989).
25. Robens, J.F., Piegorsch, W.W., and Schueler, R.L. Methods in testing for carcinogenicity. *Principles and Methods of Toxicology* (2nd edn.), A.W. Hayes, ed. New York: Raven Press, 251-273 (1989).
26. Rao, G.N., Piegorsch, W.W., Crawford, D.D., Edmondson, J. and Haseman, J.K. Influence of viral infections on body weight, survival and tumor prevalences of B6C3F$_1$ (C7BL/6N × C3H/HEN) mice in carcinogenicity studies. *Fundamental and Applied Toxicology* **13**, 156-164 (1989).
27. Piegorsch, W.W., Zimmermann, F.K., Fogel, S., Whittaker, S.G., and Resnick, M.A. Quantitative approaches for assessing chromosome loss in *Saccharomyces cerevisiae*: general methods for analyzing downturns in dose response. *Mutation Research* **224**, 11-29 (1989).
28. Whittaker, S.G., Zimmermann, F.K., Dicus, B., Piegorsch, W.W., Fogel, S., and Resnick, M.A. Detection of induced chromosome loss in *Saccharomyces cerevisiae* – An interlaboratory study. *Mutation Research* **224**, 31-78 (1989).
29. Piegorsch, W.W. and Casella, G. The early use of matrix diagonal increments in statistical problems. *SIAM Review* **31**, 428-434 (1989); Erratum: Inverting a sum of matrices. *SIAM Review* **32**, 470 (1990).
30. Piegorsch, W.W. and Bailer, A.J. Optimal design allocations for estimating area under curves for studies employing destructive sampling. *Journal of Pharmacokinetics and Biopharmaceutics* **17**, 493-507 (1989).
31. Piegorsch, W.W. Durand's rules for approximate integration. *Historia Mathematica* **16**, 324-333 (1989).
32. Bailer, A.J. and Piegorsch, W.W. MSE considerations when using quadrature rules. *Proceedings of the American Statistical Association, Biopharmaceutical Section,* 177-182 (1989).
33. Piegorsch, W.W. One-sided significance tests for generalized linear models under dichotomous response. *Biometrics* **46**, 309-316 (1990).

Publications (cont'd)

34. Whittaker, S.G., Zimmermann, F.K., Dicus, B., Piegorsch, W.W., Resnick, M.A., and Fogel, S. Detection of induced chromosome loss in *Saccharomyces cerevisiae* – An interlaboratory assessment of 12 chemicals. *Mutation Research* **241**, 225-242 (1990).

35. Piegorsch, W.W. Maximum likelihood estimation for the negative binomial dispersion parameter. *Biometrics* **46**, 863-867 (1990).

36. Whittaker, S.G., Moser, S.F., Maloney, D.H., Piegorsch, W.W., Resnick, M.A., and Fogel, S. The detection of mitotic and meiotic chromosome gain in the yeast *Saccharomyces cerevisiae*: Effects of methylbenzimidazol-2-YL carbamate, methyl methanesulfonate, ethyl methane sulfonate, dimethyl sulfoxide, propionitrile and cyclophosphamide monohydrate. *Mutation Research* **242**, 231-258 (1990).

37. Piegorsch, W.W. Fisher's contributions to genetics and heredity, with special emphasis on the Gregor Mendel controversy. *Biometrics* **46**, 915-924 (1990).

38. Bailer, A.J. and Piegorsch, W.W. Estimating integrals using quadrature methods with an application in pharmacokinetics. *Biometrics* **46**, 1201-1211 (1990).

39. Piegorsch, W.W. Review of "Statistical Evaluation of Mutagenicity Test Data," D.J. Kirkland, ed. *Statistics in Medicine* **10**, 156-158 (1991).

40. Piegorsch, W.W. Multiple comparisons for analyzing dichotomous response data. *Biometrics* **47**, 45-52 (1991).

41. Piegorsch, W.W. and Haseman, J.K. Per-litter analyses for studies of developmental toxicity. *Statistical Methods in Toxicology*, L. Hothorn, ed. Lecture Notes in Medical Informatics, Vol. **43**, Heidelberg: Springer-Verlag, 86-95 (1991).

42. Piegorsch, W.W. and Zeiger, E. Measuring intra-assay agreement for the Ames *Salmonella* assay. *Statistical Methods in Toxicology*, L. Hothorn, ed. Lecture Notes in Medical Informatics, Vol. **43**, Heidelberg: Springer-Verlag, 35-41 (1991).

43. Generoso, W.M., Shourbaji, A.G., Piegorsch, W.W., and Bishop, J.B. Developmental responses of zygotes exposed to similar mutagens. *Mutation Research* **250**, 439-446 (1991).

44. Piegorsch, W.W. and Haseman, J.K. Statistical methods for analyzing developmental toxicity data. *Teratogenesis, Carcinogenesis, and Mutagenesis* **11**, 115-133 (1991).

45. Lockhart, A.C., Bishop, J.B., and Piegorsch, W.W. Issues regarding data acquisition and analysis in the dominant lethal assay. *Proceedings of the American Statistical Association, Biopharmaceutical Section,* 234-237 (1991).

46. Piegorsch, W.W., Carr, G.J., Portier, C.J., and Hoel, D.G. Concordance of carcinogenic response between rodent species: Potency dependence and potential underestimation. *Risk Analysis* **12**, 115-121 (1992).

47. Gutierrez-Espeleta, G.A., Hughes, L.A., Piegorsch, W.W., Shelby, M.D., and Generoso, W.M. Acrylamide: Dermal exposure produces genetic damage in male mouse germ cells. *Fundamental and Applied Toxicology* **18**, 189-192 (1992).

Publications (cont'd)

48. Piegorsch, W.W. Complementary log regression for generalized linear models. *American Statistician* **46**, 94-99 (1992).
49. Lockhart, A.C., Piegorsch, W.W., and Bishop, J.B. Assessing overdispersion and dose response in the male dominant lethal assay. *Mutation Research* **272**, 35-58 (1992).
50. Piegorsch, W.W. Non-parametric methods to assess non-monotone dose response: Applications to genetic toxicology. *Order Statistics and Nonparametrics: Theory and Applications*, P.K. Sen and I.A. Salama, eds. Amsterdam: North-Holland, 419-430 (1992).
51. Piegorsch, W.W. and Taylor, J.A. Statistical methods for assessing environmental effects on human genetic disorders. *Environmetrics* **3**, 396-384 (1992).
52. Dinse, G.E., Boos, D.D., and Piegorsch, W.W. Confidence statements about the time range over which survival curves differ. *Applied Statistics* **42**, 21-30 (1993).
53. Piegorsch, W.W. and Bailer, A.J. Minimum mean-square error quadrature. *Journal of Statistical Computation and Simulation* **46**, 217-234 (1993).
54. Generoso, W.M. and Piegorsch, W.W. Dominant lethal tests in male and female mice. *Male Reproductive Toxicology*, R.E. Chapin and J.J. Heindel, eds. Methods in Toxicology, Vol. **3**, New York: Academic Press, 124-141 (1993).
55. Thomas, D. C., Nguyen, D. C., Piegorsch, W.W., and Kunkel, T. A. Relative rates of mutagenic translesion synthesis on the leading and lagging strands during replication of UV-irradiated DNA in a human cell extract. *Biochemistry* **32**, 11476-11482 (1993).
56. Evans, J.C. and Piegorsch, W.W. Environmental biometrics. *Environmetrics* **4**, 369-379 (1993).
57. Piegorsch, W.W. Biometrical methods for testing dose effects of environmental stimuli in laboratory studies. *Environmetrics* **4**, 483-505 (1993).
58. Piegorsch, W.W. Environmental Biometry: Assessing impacts of environmental stimuli via animal and microbial laboratory studies. *Handbook of Statistics 12: Environmental Statistics*, G.P. Patil and C.R. Rao, eds. New York: North-Holland/Elsevier, 535-559 (1994).
59. Piegorsch, W.W. and Bailer, A.J. Statistical approaches for analyzing mutational spectra: Some recommendations for categorical data. *Genetics* **136**, 403-416 (1994).
60. Piegorsch, W.W., Lockhart, A.-M.C., Margolin, B.H., Tindall, K.R., Gorelick, N.J., Short, J.M., Carr, G.J., Thompson, E.D., and Shelby, M.D. Sources of variability from a *lacI* transgenic mouse mutation assay. *Environmental and Molecular Mutagenesis* **23**, 17-31 (1994).
61. Piegorsch, W.W., Weinberg, C.R., and Taylor, J.A. Non-hierarchical logistic models and case-only designs for assessing susceptibility in population-based case-control studies. *Statistics in Medicine* **13**, 153-162 (1994).

Publications (cont'd)

62. Piegorsch, W.W. Statistical models for genetic susceptibility in toxicological and epidemiological investigations. *Environmental Health Perspectives* **102**, suppl. 1, 77-82 (1994).

63. Margolin, B.H., Kim, B.S., Smith, M.G., Fetterman, B.A., Piegorsch, W.W., and Zeiger, E. Some comments on potency measures in mutagenicity research. *Environmental Health Perspectives* **102**, suppl. 1, 91-94 (1994).

64. Piegorsch, W.W. Combining environmental information. *Environmental Health Perspectives* **102**, 222-225 (1994).

65. Robens, J.F., Calabrese, E.J., Piegorsch, W.W., Schueler, R.L., and Hayes, A.W. Principles of testing for carcinogenicity. *Principles and Methods of Toxicology* (3rd edn.), A.W. Hayes, ed. New York: Raven Press, 697-728 (1994).

66. Haseman, J.K. and Piegorsch, W.W. Statistical analysis of developmental toxicity data. *Developmental Toxicology* (2nd edn.), C. Kimmel and J. Buelke-Sam, eds. New York: Raven Press, 349-361 (1994).

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74. Piegorsch, W.W. and Cox, L.H. Combining environmental information II: Environmental epidemiology and toxicology. *Environmetrics* **7**, 309-324 (1996).

75. Green, A.S., Chandler, G.T., and Piegorsch, W.W. Stage-specific toxicity of sediment-associated chlorpyrifos to a marine, infaunal copepod. *Environmental Toxicology and Chemistry* **15**, 1182-1231 (1996).

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Publications (cont'd)

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95. Bailer, A.J. and Piegorsch, W.W. Quantitative potency estimation to measure risk with bio-environmental hazards. *Handbook of Statistics 18: Bioenvironmental and Public Health Statistics*, P.K. Sen and C.R. Rao, eds. New York: North-Holland/Elsevier, 441-463 (2000).
96. Bailer, A.J. and Piegorsch, W.W. From quantal counts to mechanisms and systems: The past, present and future of biometrics in environmental toxicology (Editors' Invited Paper). *Biometrics* **56**, 327-336 (2000).
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99. Nitcheva, D. and Piegorsch, W.W. Hierarchical statistical modeling in environmental toxicology. *Proceedings of the American Statistical Association, Section on Statistics and the Environment,* 111-118 (2000).
100. Piegorsch, W.W. Review of "Statistics and Experimental Design for Toxicologists, Third Edition," by S.C. Gad. *American Statistician* **55**, 81 (2001).
101. Garren, S.T., Smith, R.L., and Piegorsch, W.W. Bootstrap goodness-of-fit test for the beta-binomial model. *Journal of Applied Statistics* **28**, 561-571 (2001).
102. Turner, S.D., Tinwell, H., Piegorsch, W.W., Schmezer, P., and Ashby, J. The male rat carcinogens limonene and sodium saccharin are not mutagenic to male BigBlue™ rats. *Mutagenesis* **16** (4), 329-332 (2001).
103. Piegorsch, W.W. and Richwine, K.A. Large-sample pairwise comparisons among multinomial proportions with an application to analysis of mutant spectra. *Journal of Agricultural, Biological, and Environmental Statistics* **6** (3), 305-325 (2001).

Publications (cont'd)

104. El-Shaarawi, A.H. and Piegorsch, W.W., eds. *Encyclopedia of Environmetrics*, Vols. 1 to 4. Chichester: John Wiley & Sons (2002).

105. Piegorsch, W.W. Beta-binomial distribution. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **1**, 173-175 (2002).

106. Piegorsch, W.W. Binary data. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **1**, 175-177 (2002).

107. Piegorsch, W.W. Clean Water Act, U.S. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **1**, 350-352 (2002).

108. Piegorsch, W.W. Dispersion parameter. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **1**, 540-544 (2002).

109. Piegorsch, W.W. Distribution function. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **1**, 552-553 (2002).

110. West, R.W. and Piegorsch, W.W. Extra risk. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **2**, 731-732 (2002).

111. Piegorsch, W.W. Geometric mean. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **2**, 898-899 (2002).

112. Piegorsch, W.W. Joint action models. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **2**, 1098-1102 (2002).

113. Piegorsch, W.W. Maximum likelihood estimation. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **3**, 1234-1235 (2002).

114. Piegorsch, W.W. Multinomial distribution. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **3**, 1311-1312 (2002).

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117. Piegorsch, W.W. Quantal response data. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **3**, 1647-1649 (2002).

118. Piegorsch, W.W. Random effects. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **3**, 1672-1674 (2002).

Publications (cont'd)

119. Piegorsch, W.W. Sensitivity and specificity. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **4**, 1982-1983 (2002).
120. Piegorsch, W.W. z-Statistics. *Encyclopedia of Environmetrics*, A.H. El-Shaarawi and W.W. Piegorsch, eds. Chichester: John Wiley & Sons, **4**, 2391-2392 (2002).
121. Piegorsch, W.W. and Edwards, D. What shall we teach in environmental statistics? (with discussion). *Environmental and Ecological Statistics* **9**, 125-150 (2002).
122. Tu, W. and Piegorsch, W.W. Empirical Bayes analysis for a hierarchical Poisson generalized linear model. *Journal of Statistical Planning and Inference* (in press).
123. Simmons, S.J., Piegorsch, W.W., Nitcheva, D., and Zeiger, E. Combining environmental information via hierarchical modeling: An example using mutagenic potencies. *Environmetrics* (in press).

Technical reports

Papers from the Biometrics Unit, Cornell University, Ithaca, NY:

1. Aref, S. and Piegorsch, W.W. Analyzing experimental data by regression × SAS. Paper number BU-705-M.
2. Piegorsch, W.W. A note on confidence bands in segmented linear regression. Paper number BU-734-M.
3. Piegorsch, W.W. On the moments of ratio-based estimators in join point estimation. Paper number BU-757-M.
4. Piegorsch, W.W. Confidence intervals on the join point in segmented regression. Paper number BU-785-M.
5. Piegorsch, W.W. and Casella, G. Empirical Bayes estimation for generalized linear models. Paper number BU-1067-M.

Papers from the Library, National Institute of Environmental Health Sciences, Research Triangle Park, NC:

6. Piegorsch, W.W. Regression confidence bands for exponential family models. Library Accession number 6189.
7. Hughes-Oliver, J.M. and Piegorsch, W.W. Bayesian hypothesis testing for umbrella alternatives, with application to genotoxicity assays. Library Accession number 6604.

Technical Reports from the National Institute of Statistical Sciences, Research Triangle Park, NC:

8. Cox, L.H. and Piegorsch, W.W. Combining environmental information: Environmetric research in ecological monitoring, epidemiology, toxicology, and environmental data reporting. Technical Report #12.

Technical Reports from the Department of Statistics, University of South Carolina, Columbia, SC:

9. Piegorsch, W.W. Annotated Computer Outputs for Linear Regression and ANOVA using SAS®. Report number 177.

Technical reports (cont'd)

10. Piegorsch, W.W. and Padgett, W.J. Notes on Sequential Analysis for a Course in Mathematical Statistics. Report number 180.
11. Piegorsch, W.W. Tables of *P*-values for *t*- and Chi-square Reference Distributions. Report number 194.
12. Piegorsch, W.W. Notes on Minimum Variance Point Estimation for a Course in the Theory of Statistical Inference. Report number 195.
13. Piegorsch, W.W. Notes and Extensions for a Course in GeneralizedLinear Models. Report number 199.
14. Pan, W. and Piegorsch, W.W. Confidence bands for low-dose risk estimation with exponential data. Report number 203.
15. Edwards, D. and Piegorsch, W.W. Notes on Temporal and Spatial Analysis for a Course in Environmetrics. Report number 206.

Presentations

1. Contributed paper: On the moments of ratio-based estimators in join point estimation. Joint Statistical Meetings, Cincinnati, Ohio; 16 August 1982.
2. Contributed paper: Regularity conditions, asymptotics, and the exponential class. Joint Statistical Meetings, Toronto, Canada; 18 August 1983.
3. Contributed paper: Admissible and optimal confidence bands in simple linear regression. Joint Statistical Meetings, Philadelphia, Pennsylvania; 14 August 1984.
4. Invited seminar: Selection of confidence bands in linear regression. North Carolina State University Department of Statistics, Raleigh, North Carolina; 9 November 1984.
5. Contributed paper: The early use of diagonal increments in statistical problems. Second SIAM Conference on Applied Linear Algebra, Raleigh, North Carolina; 30 April 1985.
6. Invited seminar: Applications of the relationships between set estimators and confidence bands in simple linear regression. North Carolina Chapter, American Statistical Association, Research Triangle Park, North Carolina; 25 September 1986.
7. Contributed paper: Testing synergistic effects for simultaneous exposures with stratified dichotomous response. XIIIth International Biometric Conference, Seattle, Washington; 28 July 1986.
8. Invited seminar: Modeling departures from simple independent action in multi-factor tables of proportions.
   - New South Wales Branch, Statistical Society of Australia, Sydney, Australia; 19 May 1987.
   - Australian National University Department of Statistics, Canberra, Australia; 22 May 1987.
9. Invited seminar: Model robustness for simultaneous confidence bands. University of Sydney Department of Mathematical Statistics, Sydney, Australia; 20 May 1987.
10. Invited seminar: Allocations for interim sacrifices in long-term animal experiments. LaTrobe University Department of Statistics, Bundoora, Australia; 21 May 1987.

Presentations (cont'd)

11. Invited seminar: Shrinkage estimators for non-parametric statistical quadrature. Cornell University Statistics Center, Ithaca, New York; 13 September 1989.
12. Invited paper: Fisher's contributions to genetics and heredity, with special emphasis on the Gregor Mendel controversy. International Biometric Society Eastern North American Regional Meeting, Baltimore, Maryland; 3 April 1990.
13. Invited seminar: Poisson and binomial regression confidence bands. Miami University Department of Mathematics and Statistics, Oxford, Ohio; 17 May 1990.
14. Invited paper: Per-litter analysis for studies of developmental toxicology. 30th Congress of the European Society of Toxicology — EUROTOX '90, Leipzig, East Germany; 14 September 1990.
15. Contributed paper: Measuring intra-assay agreement for the Ames *Salmonella* assay. 30th Congress of the European Society of Toxicology — EUROTOX '90, Leipzig, East Germany; 14 September 1990.
16. Invited seminar: Statistical approaches for assessing chromosome loss. Institute of Epidemiology and Biometry, German Cancer Research Center, Heidelberg, West Germany; 27 September 1990.
17. Invited seminar: Complementary log regression. North Carolina Chapter, American Statistical Association, Research Triangle Park, North Carolina; 20 February 1991.
18. Invited seminar: Assessing gene-environment interactions in case-control studies. University of North Carolina Environmental Biostatistics Training Program, Chapel Hill, North Carolina; 27 March 1991.
19. Invited paper: Statistical models for genetic susceptibility in toxicological and epidemiological investigations. International Biostatistics Conference in the Study of Toxicology, University of Tokyo, Japan; 25 May 1991.
20. Invited paper: Statistical methods for assessing gene-environment interactions. Joint Statistical Meetings, Atlanta, Georgia; 21 August 1991.
21. Invited paper: Non-parametric methods to assess non-monotone dose responses. International Conference on Order Statistics and Non-parametrics: Theory and Applications, Alexandria University, Egypt; 20 September 1991.
22. Invited seminar: Multiple comparison procedures for dichotomous endpoints. Working Group on Chemical-Pharmaceutical Research, International Biometric Society (German Region), Heidelberg, Germany; 23 September 1991.
23. Invited seminar: Empirical Bayes estimation for generalized linear models.
    - Medical College of Virginia Department of Biostatistics, Richmond, Virginia; 21 February 1992.
    - University of Georgia Department of Statistics, Athens, Georgia; 7 April 1994.
24. Invited presentation: Sensitivity of genotoxicity assays. Biology/Statistics Workshop on Mutation Assays in Transgenic Mice, Cincinnati, Ohio; 10 June 1992.

Presentations (cont'd)

25. Invited paper: Statistics in environmental health: Animal and microbial studies.
    - American Statistical Association Summer Research Conference in Statistics, Flat Rock, North Carolina; 13 June 1992.
    - North Carolina State University Department of Statistics, Raleigh, North Carolina; 28 August 1992.
    - International Conference on Environmental Biometrics, University of Sydney, Australia; 15 December 1992.
    - Department of Epidemiology & Biostatistics, University of South Carolina, Columbia, South Carolina; 18 November 1993.
    - Department of Statistics, Virginia Polytechnic Institute and State University, Blacksburg, Virginia; 9 March 1995.
26. Invited discussion: Statistical methods for the detection of interactions between drugs. Joint Statistical Meetings, Boston, Massachusetts; 12 August 1992.
27. Invited paper: Statistical methods for analyzing dose response with overdispersed discrete data. Joint Statistical Meetings, Boston, Massachusetts; 13 August 1992.
28. Invited paper: Simultaneous regression confidence bands for count data.
    - Department of Biostatistics, University of North Carolina, Chapel Hill, North Carolina; 9 September 1992.
    - Department of Statistics, University of North Carolina, Chapel Hill, North Carolina; 14 September 1992.
    - Department of Statistics, University of South Carolina, Columbia, South Carolina; 24 September 1992.
    - Delaware Chapter, American Statistical Association, Wilmington, Delaware; 12 November 1992.
29. Invited lecture: Statistical design of dose-response assays on animals and microbes. Sydney Water Board Lecture Series: "Assessing Impacts of Pollutants on Environmental Health", Sydney, Australia; 16 December 1992.
30. Invited lecture: Statistical analysis of dose-response data — Estimation and multiple comparisons.
    - Sydney Water Board Lecture Series: "Assessing Impacts of Pollutants on Environmental Health", Sydney, Australia; 16 December 1992.
    - International Biometric Society Caribbean, Central American, Colombian and Venezuelan Network Meeting, Center for Research and Instruction in Tropical Agronomy, Turrialba, Costa Rica; 30 June 1993.
31. Invited lecture: Statistical analysis of dose-response — Testing. Sydney Water Board Lecture Series: "Assessing Impacts of Pollutants on Environmental Health", Sydney, Australia; 18 December 1992.
32. Invited lecture: An introduction to statistics in aquatic toxicology. Sydney Water Board Lecture Series: "Assessing Impacts of Pollutants on Environmental Health", Sydney, Australia; 18 December 1992.
33. Invited presentation: Sources of variability in data from transgenic mouse mutagenicity assays. Second Biology/Statistics Workshop on Mutation Assays in Transgenic Mice, Norfolk, Virginia; 17 April 1993.

Presentations (cont'd)

34. Invited paper: Assessing the impacts of environmental stimuli via animal and microbial laboratory studies. International Biometric Society Caribbean, Central American, Colombian and Venezuelan Network Meeting, Center for Research and Instruction in Tropical Agronomy, Turrialba, Costa Rica; 30 June 1993.
35. Invited lecture: Statistics in application: Some biomedical examples. American Statistical Association Quantitative Literacy Workshop-III, A Data-Driven Curriculum, Columbia, SC; 25 March 1994.
36. Invited paper: Sources of variability in transgenic mutation assays: Implications for study design. 25th Annual Meeting, Environmental Mutagen Society, Portland, OR; 8 May 1994.
37. Invited paper: Assessing gene × environment interactions: Implications for study design. Sixth Conference of the International Society for Environmental Epidemiology, Research Triangle Park, NC; 20 September 1994.
38. Invited seminar: Environmental biometry: Quantitative Methods for Environmental Data. Department of Environmental Health Sciences, University of South Carolina, Columbia, South Carolina; 9 April 1996.
39. Invited paper: Interactive Statistics on the Internet: Applications in Environmental Biology. 28th Symposium on the Interface–Computing Science and Statistics, Sydney, Australia; 10 July 1996.
40. Invited paper: Combining Environmental Information: Environmental Monitoring, Measurement and Assessment. Sydney International Statistics Congress, Sydney, Australia; 11 July 1996.
41. Invited paper: Quantifying environmental risk via low-dose extrapolation. Joint Statistical Meetings, Dallas, Texas; 12 August 1998.
42. Invited roundtable leader: Constructing/maintaining a course in environmental statistics. Joint Statistical Meetings, Dallas, Texas; 12 August 1998.
43. Invited roundtable leader: Constructing/maintaining a course in bioenvironmental and ecological statistics. International Biometric Society Eastern North American Regional Meeting, Atlanta, Georgia; 29 March 1999.
44. Invited paper: Empirical Bayes estimation for log-linear regression and extended parametric regression models. International Biometric Society Eastern North American Regional Meeting, Atlanta, Georgia; 30 March 1999.
45. Invited paper: Hierarchical Statistical Modeling in Environmental Toxicology.
    - Workshop on Hierarchical Modeling in Environmental Statistics, Columbus, Ohio; 14 May 2000.
    - International Conference on Statistical Challenges in Environmental Health Problems, Fukuoka City, Japan, 30 August 2001.
46. Invited panel member: Ethics in Research. Undergraduate Student Research Intern Program, University of South Carolina, Columbia, South Carolina; 12 July 2000.
47. Invited seminar: Extended logistic regression via the Heckman-Willis model, or 'When is a trend a trend?' University of Florida Department of Statistics, Gainesville, Florida; 15 February 2001.

Presentations (cont'd)

48. Invited paper (Special Contributed Session): Assessing environmental risk via low-dose benchmark estimation. International Biometric Society Eastern North American Regional Meeting, Charlotte, North Carolina, 28 March 2001.
49. Invited panelist: Scientific predictions of social and technical change. University of South Carolina Science Studies Group, Columbia, South Carolina, 25 February 2002.

Sessions at Professional Meetings

1. Session chair: "Methods" (Sponsor: ASA Statistical Computing Section). Joint Statistical Meetings, Toronto, Canada; 17 August 1983.
2. Session organizer: "Random effects/measurement error methods for environmental applications" (Sponsor: ASA Section on Statistics & the Environment). International Biometric Society Eastern North American Regional Meeting, Houston, Texas; 26 March 1991.
3. Session chair: "Environmental monitoring and sampling strategies" (Sponsor: ASA Section on Statistics & the Environment). Joint Statistical Meetings, Atlanta, Georgia; 20 August 1991.
4. Session organizer: "Ecosystem monitoring and assessment" (Sponsor: ASA Section on Statistics & the Environment). International Biometric Society Eastern North American Regional Meeting, Cincinnati, Ohio; 24 March 1992.
5. Session organizer: "Statistics and the environment: Incorporating social, legal, and economic issues" (Sponsor: Southern Regional Council on Statistics). American Statistical Association Summer Research Conference in Statistics, Galveston, Texas; 6 June 1993.
6. Session chair: "Models & Monte Carlo" (Sponsor: ASA Section on Statistics & the Environment). Joint Statistical Meetings, San Francisco, California; 11 August 1993.
7. Session organizer: "Environmetrics for Aquatic and Atmospheric Studies." CHESM-93, Satellite Meeting to the 49th ISI Session, Bologna, Italy; 23 August 1993.
8. Invited Moderator: "DNA Evidence in the Courtroom" (Sponsor: S.C. Chapter of ASA). 25th Annual Meeting, South Carolina Chapter, American Statistical Association, Columbia, South Carolina; 21 April 1995.
9. Session chair/organizer: "Ecotoxicology, Bio-Accumulation and Risk Analysis" (Sponsor: Statistical Society of Australia). Sydney International Statistics Congress, Sydney, Australia; 11 July 1996.
10. Session chair: "Environmental Monitoring" (Sponsor: ASA Section on Statistics & the Environment). Joint Statistical Meetings, Chicago, Illinois; 5 August 1996.
11. Session organizer: "The Future of Environmental Statistics" (Sponsor: ASA Section on Statistics & the Environment). Joint Statistical Meetings, Anaheim, California; 12 August 1997.
12. Invited moderator: "College Bowl Quarterfinals" (Sponsor: Mu Sigma Rho and ASA Section on Statistical Education). Joint Statistical Meetings, Baltimore, Maryland, 10 August 1999.

Sessions (cont'd)

13. Session chair: "Estimation and Inference in Toxicity and Carcinogenicity Studies" (Sponsor: ENAR and I.M.S.). International Biometric Society Eastern North American Regional Meeting, Charlotte, North Carolina, 26 March 2001.
14. Session chair: "Applications of Statistics in Market Research and Related Areas." University of South Carolina Department of Statistics 15th Anniversary Alumni Conference, Columbia, South Carolina, 31 March 2001.
15. Session chair: "Invited paper Session (5)." International Conference on Statistical Challenges in Environmental Health Problems, Fukuoka City, Japan, 1 September 2001.

APPENDIX E

Dr. David M. Rocke
Curriculum Vitae

DAVID M. ROCKE

Curriculum Vitae
January 2002

Department of Applied Science
University of California
Davis, California 95616
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PERSONAL

Birth date: June 4, 1946
Married, two children
U.S. Citizen

EDUCATION

Ph.D., University of Illinois, Chicago, 1972 (Mathematics)
Supplemental Coursework, University of Chicago, 1977–79 (Statistics)
M.A., University of Illinois, Chicago, 1968 (Mathematics)
A.B., Shimer College, 1966 (Mathematics and Physics)

HONORS

National Merit Scholarship, 1964–66.
Graduated "With Distinction" from Shimer College, 1966.
National Science Foundation Graduate Fellowship, 1968–71.
Fellow of the Royal Statistical Society, 1979.
Youden Prize, Chemical Division, American Society for Quality Control, 1982.
Award for Interlaboratory Testing, American Statistical Association, 1985.
Shewell Award, Chemical and Process Industries Division, American Society for Quality Control, 1987.
Fellow of the American Statistical Association, 1995.
Statistics in Chemistry Award, American Statistical Association, 1997.
Elected to Membership in the International Statistical Institute, 1997.
Distinguished Service Award, Division of Molecular Orthopaedics, University of Pennsylvania, 2000.

EMPLOYMENT

Professor, Department of Applied Science, University of California, Davis, 2000–present, Vice-Chair, 2001–present.
Professor, Department of Epidemiology and Preventive Medicine, UC Davis School of Medicine, 1997–present; Acting Director of Biostatistics 1997–2000.
Co-Director, Center for Image Processing and Integrated Computing, UC, Davis, 1996–present.
Director, Center for Digital Security, UC Davis, 2001–present.
Professor Graduate School of Management, UC Davis, 1986–2000. Associate Professor, 1980–1986.
Director, Center for Statistics in Science and Technology, UC Davis, 1995–99.
Academic Visitor, Department of Mathematics, Imperial College, London, 1987–1988.
University Professor of Business Administration, Governors State University, 1974–80.
Lecturer (visiting), Department of Mathematics, University of Illinois, Chicago, 1972–74.
Scientific Computer Programmer, Argonne National Laboratory, Summers 1965–69.

COURSES TAUGHT

Introductory Statistics
Regression Analysis and Linear Models
Experimental Design
Time Series Analysis and Forecasting
Bootstrap Methods
Mathematical Physics
Management Science
Production and Operations Management
Program Evaluation
Quality and Productivity Improvement
Technology Management
Introduction to Computing
Computer Architecture/Assembly Language
Other Mathematics courses

RECENT GRANTS AND CONTRACTS

Air Force Office of Scientific Research, 2001–03, Center for Digital Security, PI with two Co-PI's.

University of California Life Sciences Informatics Program and Surromed Inc., 2000–2002, Prediction, Classification, and Analysis of Highly Multivariate Biomedical Laboratory Data, (with David Woodruff).

National Science Foundation, 1998–02, Robust Multivariate Analysis and Outlier Identification in Massive Data Sets (with David Woodruff).

National Institutes of Health, National Institute of Environmental Health Sciences, 1988–2005, Statistical analysis of toxics measurement data.

National Science Foundation, 1997–02, PI for UC Davis component of the National Partnership for Advanced Computing Infrastructure (Supercomputer) project centered at UCSD, 3 Co-PI's at UC Davis.

US Environmental Protection Agency, 1997–02, Statistical Methods and Computer Implementation for Precision Determination for Low Level Analytes.

National Aeronautics and Space Administration, 1998–01, Towards Real-Time Vector Field Visualization for Massive and Multi-Source Data using Hierarchies, Co-PI, Bernd Hamann PI.

Lawrence Livermore National Laboratory, 1998–01, Hierarchical Methods for the Representation and Visualization of Terascale Data Coupled with Data Mining and Immersive Environments. Co-PI, Bernd Hamann PI.

National Institutes of Health, National Cancer Institute, 1997–01, BPH: Molecular Biology of P53 and BCL-2 Alterations, Statistician, Paul Gumerlock PI.

National Institutes of Health, National Cancer Institute, 1998–01, Protein Interaction with the N-terminus of the Androgen Receptor, Statistician, Paul Gumerlock PI.

National Institutes of Health, National Cancer Institute, 1998–01, Functions of Different P53 Mutations in Prostate Cancer, Statistician.

National Science Foundation, 1998–99, Applications of Parallel Computing in Computer Science, Computer Engineering, and Analysis and Visualization of Massive Data Sets (CISE Equipment Grant). PI with two Co-PI's.

National Science Foundation, 1995–99, Center for Statistics in Science and Technology, Group Infrastructure Grant. Project director with 5 Co-PI's and 6 Faculty Associates.

MEMBERSHIP IN PROFESSIONAL SOCIETIES

American Association for the Advancement of Science
American Mathematical Society
American Society for Quality Control

American Statistical Association (Fellow)
Association for Computing Machinery
Bernoulli Society
Biometric Society
Institute of Mathematical Statistics
International Association for Statistical Computing
International Society for Computational Biology (Treasurer 2002, Board of Directors 2002–2004)
International Statistical Institute
Mathematical Association of America
Royal Statistical Society (Fellow)
Society for Industrial and Applied Mathematics

EDITORIAL WORK

Associate Editor, *Journal of Business and Economic Statistics*, 1986–1995
Associate Editor, *Biometrics*, 1997–2000
Associate Editor, *Metrika*, 1998–
Reviewer for: *American Journal of Political Science, Annals of Statistics, Applied Statistics, Australian Journal of Statistics, Bioinformatics, Biometrics, Biometrika, BIT, Canadian Journal of Statistics, Communications in Statistics, Computational Statistics and Data, Analysis, International Studies Quarterly, Irwin, John Wiley, Journal of Applied Statistical Science, Journal of Computational Biology, Journal of Conflict Resolution, Journal of Immunological Methods, Journal of Forecasting, Journal of Multivariate Analysis, Journal of Nonparametric Statistics, Journal of Quality Technology, Journal of Statistical Computation and Simulation, Journal of Statistical Planning and Inference, Journal of the American Statistical Association, Journal of the Royal Statistical Society B, National Science Foundation, Naval Research Logistics, SIAM Journal on Scientific and Statistical Computing, The Statistician, Technometrics, University of Michigan Press, West, World Politics.*

BOOKS

1995 George W. Downs and David M. Rocke, *Optimal Imperfection? Domestic Uncertainty and Institutions in International Relations,* Princeton: Princeton University Press.
1990 George W. Downs and David M. Rocke, *Tacit Bargaining, Arms Races, and Arms Control*, Ann Arbor: University of Michigan Press.

STATISTICAL THEORY AND METHODOLOGY

2002 Danh Nguyen and David M. Rocke, "Classification in High Dimension with Application to DNA Microarray Data," submitted for publication.
2002 David M. Rocke and David L. Woodruff, "Multivariate Outlier Detection and Cluster Identification," submitted for publication.
2002 Johanna Hardin and David M. Rocke, "Robust Distances," submitted for publication.
2002 David M. Rocke and Jian Dai, "Sampling and Subsampling for Cluster Analysis in Data Mining, with Applications to Sky Survey Data," submitted for publication.
2002 Geoffrey Jones and David M. Rocke "Multivariate Survival Analysis with Doubly Censored Data: Application to the Assessment of Accutane Treatment for Fibrodysplasia Ossificans Progressiva," *Statistics in Medicine*, in press
2001 David M. Rocke and David L. Woodruff "Discussion of `Multivariate Outlier Detection and Robust Covariance Matrix Estimation,'" *Technometrics*, **43**, 300–303.
2001 Geoffrey Jones and David M. Rocke "Analyte Identification in Multivariate Calibration," *Biometrics*, **57**, 571–576.
1999 Dan Coleman Xiaopeng Dong, Johanna Hardin, David M. Rocke, and David L. Woodruff, "Some Computational Issues in Cluster Analysis with No A Priori Metric," *Computational Statistics and Data Analysis*, **31**, 1–12.

1999 Geoffrey Jones and David M. Rocke "Bootstrapping in Controlled Calibration Experiments," *Technometrics*, **41**, 224–233.

1998 David M. Rocke, "Constructive Statistics: Estimators, Algorithms, and Asymptotics," *Computing Science and Statistics*, **30**, 3–14.

1998 David M. Rocke, "A Perspective on Statistical Tools for Data Mining Applications," *Proceedings of the Second International Conference on Practical Application of Knowledge Discovery and Data Mining*, 313–318.

1998 David M. Rocke, "Laboratory Quality Control," in *Encyclopedia of Biostatistics*, New York: John Wiley.

1997 David M. Rocke and Geoffrey Jones, "Optimal Design for ELISA and other forms of Immunoassay," *Technometrics*, **39**, 162–170.

1997 David M. Rocke and David L. Woodruff, "Robust Estimation of Multivariate Location and Shape," *Journal of Statistical Planning and Inference*, **57**, 245–255.

1996 David M. Rocke and David L. Woodruff, "Identification of Outliers in Multivariate Data," *Journal of the American Statistical Association*, **91**, 1047–1061.

1996 David M. Rocke, "Robustness Properties of *S*-Estimators of Multivariate Location and Shape in High Dimension," *Annals of Statistics*, **24**, 1327–1345.

1995 David M. Rocke and Michelle Pallas "Prediction of Automotive Emissions from Gasoline Composition," *Proceedings of the 1994 Spring Research Conference on Statistics in Industry and Technology*, American Statistical Association.

1995 David M. Rocke and Stefan Lorenzato, "A Two-Component Model for Measurement Error in Analytical Chemistry," *Technometrics*, **37**, 176–184.

1994 David M. Rocke and David L. Woodruff, "Multivariate Outlier Detection," in *Proceedings of the 26th Symposium on the Interface: Computing Science and Statistics*, 392–400.

1994 David L. Woodruff and David M. Rocke, "Computable Robust Estimation of Multivariate Location and Shape using Compound Estimators," *Journal of the American Statistical Association*, **89**, 888–896.

1993 David Woodruff and David M. Rocke, "Heuristic Search Algorithms for the Minimum Volume Ellipsoid," *Journal of Computational and Graphical Statistics*, **2**, 69–95.

1993 David M. Rocke, "Almost-Exact Parametric Bootstrap Calculation via the Saddle-Point Approximation," *Computational Statistics and Data Analysis*, **15**, 451–460.

1993 David M. Rocke and David L. Woodruff, "Computation of Robust Estimates of Multivariate Location and Shape," *Statistica Neerlandica*, **47**, 27–42.

1993 David M. Rocke, "On the Beta Transformation Family," *Technometrics*, **35**, 72–81.

1992 David M. Rocke and David L. Woodruff, "Computation of High-Breakdown Estimates of Multivariate Location and Shape," *Proceedings of the ASA Statistical Computing Section*, 34–39.

1992 David M. Rocke, "$\overline{X}_Q$ and R_Q Charts: Robust Control Charts," *The Statistician*, **41**, 97–104.

1992 David M. Rocke, "Estimation of Variation after Outlier Rejection," *Computational Statistics and Data Analysis*, **13**, 9–20.

1991 David M. Rocke, "Robustness and Balance in the Mixed Model," *Biometrics*, **47**, 303–309.

1990 David M. Rocke, "The Adjusted p-Chart and u-Chart for Varying Sample Sizes," *Journal of Quality Technology*, **22**, 206–209.

1990 Rudolph Grübel and David M. Rocke, "On the Cumulants of Affine Equivariant Estimators in Elliptical Families," *Journal of Multivariate Analysis*, **35**, 203–222.

1989 David M. Rocke, "Robust Control Charts," *Technometrics*, **31**, 173–184.

1989 David M. Rocke, "Bootstrap Bartlett Adjustment for Seemingly Unrelated Regression," *Journal of the American Statistical Association*, **84**, 598–601.

1987 Richard Green, David M. Rocke, and William Hahn, "Standard Errors for Elasticities: A Comparison of Bootstrap and Asymptotic Standard Errors," *Journal of Business and Economic Statistics*, **5**, 145–149.

1986 David M. Rocke and David F. Shanno, "The Scale Problem in Robust Regression M-Estimates," *Journal of Statistical Computation and Simulation*, 1986, **24**, 47–69.

1986 David M. Rocke, "Outlier Resistance in Small Samples," *Biometrika*, **73**, 175–181.

1986 David F. Shanno and David M. Rocke, "Numerical Methods for Robust Regression: Linear Models," *SIAM Journal on Scientific and Statistical Computing*, **7**, 86–97.

1984 David M. Rocke, "On Testing for Bioequivalence," *Biometrics*, **40**, 225–230.

1983 George W. Downs and David M. Rocke, "Municipal Budget Forecasting with Multivariate ARMA Models," *Journal of Forecasting*, **2**, 377–387.

1983 George W. Downs and David M. Rocke, "Designed Experiments for Classification Problems," *Journal of the Operational Research Society*, **34**, 1069–1077.

1983 George W. Downs and David M. Rocke, "Multivariate ARIMA Models and Municipal Finance," in *Applied Time Series Analysis of Economic Data*, ed. Arnold Zellner, Bureau of the Census.

1983 David M. Rocke, "Robust Statistical Analysis of Interlaboratory Studies," *Biometrika*, **70**, 421–431.

1982 David M. Rocke, "Inference for Response-Limited Time Series Models," *Communications in Statistics*, **A11**, 2587–2596.

1982 David M. Rocke, George W. Downs and Alan J. Rocke "Are Robust Estimators Really Necessary?" *Technometrics*, **24**, 95–102.

1981 David M. Rocke and George W. Downs, "Estimating the Variance of Estimators of Location: Influence, Curve, Jackknife and Bootstrap," *Communications in Statistics*, **B10**, 221–248.

1980 David M. Rocke and George W. Downs, "Time Series with Episodic Disruptions" in *Analysing Time Series*, ed. O.D. Anderson, New York: North-Holland.

1975 David M. Rocke, "p-Groups with Abelian Centralizers," *Proceedings of the London Mathematical Society*, **3**, **30**, 55–75.

MEDICINE, BIOLOGY, CHEMISTRY, ENVIRONMENTAL SCIENCE

2002 David M. Rocke, Blythe Durbin, Machelle Wilson, and Henry Kahn, "Modeling Uncertainty in Analytical Measurements for Analysis of Bioavailability," submitted for publication.

2002 Joseph A. Caruso, Björn Klaue, Bernhard Michalke, and David M. Rocke, "Analytical Methodologies for Metal Speciation," submitted for publication.

2002 Danh Nguyen and David M. Rocke, "Multi-Class Cancer Classification via Partial Least Squares with Gene Expression Profiles," submitted for publication.

2002 Danh Nguyen and David M. Rocke, "Partial Least Squares Proportional Hazard Regression for Application to DNA Microarray Data," submitted for publication.

2002 Machelle Wilson, David M. Rocke, Blythe Durbin, and Henry Kahn, "Application to Environmental Monitoring of a Two-Component Model for Chemical Analytical Error," submitted for publication.

2002 Danh Nguyen and David M. Rocke, "Classification of Acute Leukemia Based on DNA Microarray Gene Expressions Using Partial Least Squares," in *Methods of Microarray Data Analysis*, S. M. Lin and K. F. Johnson, eds., Kluwer, in press.

2002 Danh Nguyen and David M. Rocke, "Tumor Classification by Partial Least Squares using Gene Expression Data," *Bioinformatics*, in press.

2001 David M. Rocke and Blythe Durbin, "A Model for Measurement Errors for Gene Expression Arrays," *Journal of Computational Biology*, **8**, 557–569.

2000 Jian Dai and David M. Rocke, "A GIS-Based Approach to Spatial Allocation of Area Source Solvent Emissions," *Environmental Modelling and Software*, **15**, 293–302.

2000 Jian Dai and David M. Rocke, "Modeling Spatial Variation in Area Source Emissions—A Poisson Regression Approach," *Journal of Agricultural, Biological and Environmental Statistics*, **5**, 7–21.

2000 Bruce N. Leistikow, Daniel C. Martin, Jeffrey Jacobs, David M. Rocke, and Kyle Noderer, "Smoking as a Risk Factor for Accident Death: A Meta-analysis of Cohort Studies," *Accident Analysis and Prevention*, **32**, 397–405.

1999 Bruce N. Leistikow, Daniel C. Martin, Jeffrey Jacobs, and David M. Rocke, "Smoking as a Risk Factor for Injury Death: A Meta-analysis of Cohort Studies," *Preventive Medicine*, **27**, 871–878.

1998 Kelli Hoover, Susan A. Alaniz, Julie L. Yee, David M. Rocke, Bruce D. Hammock, and Sean S. Duffey, "Dietary Protein and Chlorogenic Acid Effect on Baculoviral Disease of Noctuid (lepidoptera: Noctuidae) Larvae," *Environmental Entomology*, **27**, 1264–1272.

1998 Kelli Hoover, Julie L. Yee, Christine M. Schultz, David M. Rocke, Bruce D. Hammock, and Sean S. Duffey, "Effects of Plant Identity and Chemical Constituents on the Efficacy of a Baculovirus Against *Heliothis Virescens*," *Journal of Chemical Ecology*, **24**, 221–252.

1998 Frederick S. Kaplan, Jeffrey R. Sawyer, Susan Connors, Karen Keough, Eileen Shore, Francis Gannon, David Glaser, David M. Rocke, Michael A. Zasloff, and Judah Folkman, "Urinary Basic Fibroblast Growth Factor: A Biochemical Marker for Preosseous Fibroproliferative Lesions in Patients Who Have Fibrodysplasia Ossificans Progressiva," *Clinical Orthopaedics and Related Research*, **346**, 59–65

1998 David L. Glaser, David M. Rocke, and Frederick S. Kaplan, "Catastrophic Falls in Patients Who Have Fibrodysplasia Ossificans Progressiva," *Clinical Orthopaedics and Related Research*, **346**, 110–116.

1998 Michael A. Zasloff, David M. Rocke, Leslie J. Crofford, Gregory V. Hahn, and Frederick S. Kaplan, "Treatment of Patients Who Have Fibrodysplasia Ossificans Progressiva with 13-cis-Retinoic Acid (Isotretinoin)," *Clinical Orthopaedics and Related Research*, **346**, 121–129.

1998 Jeffrey R. Sawyer, John J. Klimkeiwicz, Joseph P. Iannotti, and David M. Rocke., "Mechanism for Superior Subluxation of the Glenohumeral Joint in Patients Who Have Fibrodysplasia Ossificans Progressiva," *Clinical Orthopaedics and Related Research*, **346**, 130–133.

1997 Geoffrey Jones, Monika Wortberg, David M. Rocke, and Bruce D. Hammock, "Immunoassay of Cross-Reacting Analytes," in *Immunochemical Technology for Environmental Applications*, D. S. Aga and E. M. Thurman, eds., ACS Symposium Series No. 657, 331–342, Washington, D.C.: American Chemical Society Publications.

1996 Geoffrey Jones, Monika Wortberg, Bruce D. Hammock, and David M. Rocke, "A Procedure for the Immunoanalysis of Samples Containing One or More Members of a Group of Cross-Reacting Analytes," *Analytica Chimica Acta*, **336**, 175–183.

1996 Geoffrey Jones, Monika Wortberg, Sabine B. Kreissig, Bruce D. Hammock, and David M. Rocke, "On the Application of the Bootstrap to Calibration Experiments," *Analytical Chemistry*, **68**, 763–770.

1996 Monika Wortberg, Geoffrey Jones, Sabine B. Kreissig, David M. Rocke, and Bruce D. Hammock, "An Approach to the Construction of an Immunoarray for Differentiating and Quantitating Cross Reacting Analytes," *Analytica Chimica Acta*, **319**, 291–303.

1996 Wayne Luchetti, Randolph B. Cohen, Gregory V. Hahn, David M. Rocke, Mark Helpin, Michael A. Zasloff, and Frederick S. Kaplan, "Severe Restriction in Jaw Movement Following Routine Injection of Local Anesthetic in Patients who have Fibrodysplasia Ossificans Progressiva," *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*, **81**, 21–25.

1995 Geoffrey Jones, Monika Wortberg, Sabine B. Kreissig, Bruce D. Hammock, and David M. Rocke, "Sources of Experimental Variation in Calibration Curves for Enzyme-Linked Immunosorbent Assay," *Analytica Chimica Acta*, **313**, 197–207.

1995 David M. Rocke, "Optimal Design of Quantitative Immunoassay Protocols," in *New Frontiers in Agrochemical Immunoassay*, David Kurtz, ed., Washington, DC: Association of Official Analytical Chemists, 251–259.

1995 Thomas F. Lanchoney, Randolph B. Cohen, David M. Rocke, Michael A. Zasloff, and Frederick S. Kaplan, "Permanent Heterotopic Ossification at the Injection Site Following Routine

Diphtheria-Tetanus-Pertussis Immunizations in Children who have Fibrodysplasia Ossificans Progressiva," *Journal of Pediatrics*, **126**, 762–764.

1995 Monika Wortberg, Sabine B. Kreissig, Geoffrey Jones, David M. Rocke, and Bruce D. Hammock, "An Immunoarray for the Simultaneous Determination of Multiple Triazine Herbicides," *Analytica Chimica Acta*, **304**, 339–352.

1995 Lawrence M. Kauvar, Deborah L. Higgins, Hugo O. Villar, J. Richard Sportsman. Åsa Engqvist-Goldstein, Robert Bukar, Karin E. Bauer, H. Dilley and David M. Rocke, "Predicting Ligand Binding to Proteins by Affinity Fingerprinting," *Chemistry and Biology*, **2**, 107–118.

1994 Geoffrey Jones, Monica Wortberg, Sabine B. Kreissig, David S. Bunch, Shirley Gee, Bruce Hammock, and David M. Rocke, "Extension of the Four-Parameter Logistic Model for ELISA to Multianalyte Analysis," *Journal of Immunological Methods*, **177**, 1–7.

1994 David M. Rocke, Michael Zasloff, Jeannie Peeper, Randolph Cohen, and Frederick S. Kaplan, "Age- and Joint-Specific Risk of Initial Heterotopic Ossification in Patients who have Fibrodysplasia Ossificans Progressiva," *Clinical Orthopaedics and Related Research*, **301**, 243–248.

1990 David S. Bunch, David M. Rocke, and Robert O. Harrison, "Statistical Design of ELISA Protocols," *Journal of Immunological Methods*, **132**, 247–254.

POLITICAL SCIENCE

1998 George W. Downs, David M. Rocke, and Peter N. Barsoom, "Managing the Evolution of Multilateralism," *International Organization*, **52**, 397–419.

1996 George W. Downs, David M. Rocke, and Peter N. Barsoom, "Is the Good News about Compliance Good News for Cooperation?" *International Organization*, **50**, 379–406, reprinted in *International Institutions* Lisa A Martin and Beth A Simmons, eds., 2001, Cambridge:MIT Press.

1994 George W. Downs and David M. Rocke, "Conflict, Agency, and Gambling for Resurrection: The Principal-Agent Problem Goes to War" *American Journal of Political Science*, **38**, 362–80.

1986 George W. Downs and David M. Rocke, "Tacit Bargaining and Arms Control," (1987) *World Politics*, **39**, 297–325.

1985 George W. Downs, David M. Rocke, and Randolph Siverson, "Arms Races and Cooperation," *World Politics*, **38**, 118–146, reprinted in *Cooperation under Anarchy*, Princeton University Press.

1984 George W. Downs and David M. Rocke, "Theories of Budgetary Decisionmaking and Revenue Decline," *Policy Sciences*, **16**, 329–347.

1982 George W. Downs and David M. Rocke, "Ceteris Paribus Revisited," *Political Methodology*, 43–54.

1980 George W. Downs and David M. Rocke, "Complexity, Interaction and Policy Research," *Policy Sciences*, **13**, 281–295.

1980 George W. Downs and David M. Rocke, "Bureaucracy and Juvenile Corrections," in *Determinants of Public Policy*, Thomas Dye and Virginia Gray, eds., Lexington MA: Heath-Lexington.

1979 George W. Downs and David M. Rocke, "Interpreting Heteroscedasticity," *American Journal of Political Science*, **23**, 816–828.

PATENTS

2001 David L. Woodruff and David M. Rocke, "Algorithm for Clustering Genes based on Microarray Data," (pending).

2000 David M. Rocke and Blythe P. Durbin, "A Method for Determining Measurement Error for Nucleic Acid Microarrays," 60/233,547 (pending)

2000 David M. Rocke and Danh V. Nguyen, "Analysis of Gene Expression from DNA Microarrays using Partial Least Squares," 60/233,546 (pending)

BOOK REVIEWS

Genetic Algorithms + Data Structures = Evolution Programs (3rd Edition), by Zbigniew Michalewicz, *Journal of the American Statistical Association*, 2000, **95**, 347–348.

Directions in Robust Statistics and Diagnostics, Parts I and II, edited by Werner Stahel and Sanford Weisberg, *Journal of the American Statistical Association*, 1993, **88**, 710–711.

Robust Estimation and Testing, by Robert G. Staudte and Simon J. Sheather, *International Statistical Institute Short Book Reviews*, 1991, **11**, 6.

Mixture Models: Inference and Application to Clustering, by G. J. McLachlan and K. E. Basford, *International Statistical Institute Short Book Reviews*, 1988, **8**, 26.

Analysis of Experiments with Missing Data, by Yadolah Dodge, *Technometrics*, 1987, **29**, 116.

Robust Inference, by M. L. Tiku, W. Y. Tan, N. Balakrishnan, *Technometrics*, 1987, **29**, 495–496.

INVITED PRESENTATIONS

2001 David M. Rocke, "Statistical Analysis of Gene Expression Data," Invited Presentation, Chiron, Emeryville, CA, November.

2001 David M. Rocke, "Modeling Uncertainty in Analytical Measurements for Analysis of Bioavailability," *Methodologies for Assessing Exposure to Metals: Speciation, Bioacessibility and Bioavailability in the Environment, Food and Feed*, Scientific Group on Methodology for the Safety and Evaluation of Chemicals (SGOMSEC), Schmallenberg, Germany, October.

2001 David M. Rocke, "Statistical Analysis of Gene Expression Data," Invited Presentation, The Scripps Research Institute, San Diego.

2001 David M. Rocke and Davis L. Woodruff, "Variance Functions, Transformations, and the Integrity of Statistical Inference with Biological Data," Invited Presentation, SurroMed, Inc., August.

2001 David M. Rocke, "Robust Multivariate Analysis and Outlier Detection," Invited Presentation, *Society for Industrial and Applied Mathematics Annual Meeting*, San Diego, July.

2001 David M. Rocke, "Statistical Analysis of Gene Expression Data," Invited Presentation, University of California, San Diego, June.

2001 David M. Rocke, "Statistical Analysis of Gene Expression Data," Invited Presentation, Michigan State University, May.

2001 David M. Rocke, "Statistical Analysis of Gene Expression Microarray Data," Invited Presentation, Merck, March.

2001 David M. Rocke, "Statistical Analysis of Gene Expression Microarray Data," Invited Presentation, University of Washington, February.

2001 David M. Rocke, "Statistical Analysis of Gene Expression Microarray Data," Invited Presentation, Lawrence Livermore National Laboratory, February.

2000 David M. Rocke, "Statistical Analysis of Gene Expression Microarray Data," Invited Presentation, *EUChem Conference on Bioinformatics, Cheminformatics, Datamining, and Chemometrics, Swedish Chemical Society*, Stockholm, September.

2000 David M. Rocke and David L. Woodruff, "Robust Clustering," Invited Presentation, *Controlling Complexity for Strong Stochastic Dependencies, Mathematisches Forschungsinstitut Oberwolfach*, Oberwolfach, Germany, September.

2000 David M. Rocke, David L. Woodruff, and Johanna Hardin, "Robust Cluster Analysis and Outlier Identification," Invited Presentation, *Joint Statistics Meetings 2000*, Indianapolis, August.

1999 David M. Rocke, "Robust Multivariate Analysis and Outlier Detection," Invited Presentation, Mathsoft, Inc., Seattle, November.

1999 David M. Rocke and Geoff Jones, "Bootstrapping in Controlled Calibration Experiments," Invited Presentation, *43rd Annual Fall Technical Conference, American Society for Quality, American Statistical Association*, Houston, October.

1999 David M. Rocke, "Data Mining," Invited Presentation, *Gordon Research Conference on Statistics in Chemistry and Chemical Engineering*, Plymouth, MH, July.

1999 David M. Rocke, "Robust Cluster Analysis and Outlier Identification," Invited Presentation, *Conference on Complexity Reduction in Multivariate Datasets*, Universität Dortmund, March.

1998 David M. Rocke, "Clustering and Outlier Detection in Massive, High-Dimensional Data Sets," Invited Presentation, *NIPS 98 Workshop on Mining Massive Databases: Scaling Prediction and Clustering to Massive and High Dimensional Data*, Brekenridge, CO, December.

1998 David M. Rocke, "Interdisciplinary Collaboration: Why and How?" Invited Presentation, *Society for Industrial and Applied Mathematics Meeting*, Chicago, October.

1998 David M. Rocke, "Constructive Statistics: Estimators, Algorithms, and Asymptotics," Invited Presentation, University of Illinois, Chicago, September.

1998 David M. Rocke, "Constructive Statistics: Estimators, Algorithms, and Asymptotics," Invited Presentation, Pfizer Central Research, Groton, CT, August.

1998 David M. Rocke, "A Two-Component Model for Measurement Error in Analytical Chemistry," Invited Presentation, National Institute for Standards and Technology, Gaithersburg, MD, July.

1998 David M. Rocke, "A Two-Component Model for Measurement Error in Analytical Chemistry," Invited Presentation, United States Environmental Protection Agency, Washington, DC, July.

1998 David M. Rocke, "Constructive Statistics: Estimators, Algorithms, and Asymptotics," Invited Keynote Address, *30th Symposium on the Interface: Computing Science and Statistics*, Minneapolis, MN, May.

1997 David M. Rocke, "Robust Multivariate Analysis and Outlier Detection," Invited Plenary Address, *Annual Meeting of the Belgian Statistical Society*, Mol, Belgium, October.

1997 David M. Rocke and David L. Woodruff, "Partitioning and Subsampling to Uncover Subtle Structure in Massive Data Sets," Invited Presentation, *Summer Research Institute on Data Mining*, Seattle, Washington, June.

1997 David M. Rocke, "Statistics of Measurement Error in Analytical Chemistry," Invited Presentation, *EPA Twelfth Annual Conference on Environmental Statistics*, Richmond, VA, April.

1997 David M. Rocke, "Partitioning and Subsampling to Uncover Subtle Structure in Massive Data Sets," Invited Presentation, *Approaches to the Analysis and Visualization of Massive Data Sets Workshop*, San Diego, CA, March 14 and 15.

1996 David M. Rocke, "Statistical Methods for the Identification of and Measurement of Mixtures of Similar Toxic Substances," Invited Presentation, *Superfund Basic Research Program: A Decade of Improving Health through Multidisciplinary Research*, Chapel Hill, NC, February.

1996 David M. Rocke, "A Two-Component Model for Measurement Error in Analytical Chemistry," Invited Presentation, *ASMS Fall Workshop on Limits to Confirmation, Quantitation, and Detection*, Alexandria, VA, November.

1996 David M. Rocke and David L. Woodruff, "Robust, Affine-Equivariant Cluster Analysis," Invited Presentation, DuPont, Wilmington, DE, October.

1996 George W. Downs, David M. Rocke, and Peter Barsoom, "Design and Evolution of Multilateral Agreements," Invited Presentation, *American Political Science Association Annual Meeting*, September.

1996 David M. Rocke and George W. Downs, "The Problem of Preference Change in International Security Agreements," Invited Presentation, *American Statistical Association Annual Meeting*, Chicago, August.

1996 George W. Downs, David M. Rocke, and Peter Barsoom, "Regime Design and the Depth of Cooperation," Invited Presentation, *International Studies Association Annual Meeting*, San Diego, CA, April.

1996 David M. Rocke, "Robust Scale-Free Cluster Analysis," Invited Presentation, Mathematisches Forschungsinstitut Oberwolfach, Mathematische Stochastik, Oberwolfach, Germany, March.

1996 David M. Rocke and David L. Woodruff, "Identification of Outliers in Multivariate Data", Invited Presentation, DuPont, Wilmington, DE, February.

1995 David M. Rocke, "Predictive Models for Reformulated Gasoline," Invited Presentation, Lawrence Livermore National Laboratory, Livermore, CA, August.

1995 David M. Rocke and David L. Woodruff, "Heuristic Combinatorial Search Algorithms for the Detection of Outliers in High Dimension," Invited Presentation, Universität Hannover, Hannover, Germany, March.

1995 David M. Rocke and David L. Woodruff, "Robust Estimation and the Identification of Outliers in Multivariate Data," Invited Presentation, Universität Dortmund, Dortmund, Germany, March.

1994 David M. Rocke and David L. Woodruff, "Identification of Outliers in Multivariate Data," Invited Presentation, Merrill Lynch, Princeton, NJ, September.

1994 David M. Rocke and David L. Woodruff, "Identification of Outliers in Multivariate Data," Invited Presentation, Columbia University, New York, NY, September.

1994 David M. Rocke and David L. Woodruff, "Robust Estimation and the Identification of Outliers and Leverage Points in Multivariate Data," Invited Presentation, *Symposium on Future Directions in Robust Methods and Data Analysis*, Princeton, NJ, June.

1994 David M. Rocke and David L. Woodruff, "Identification of Outliers in Multivariate Data," Invited Presentation, *26th Symposium on the Interface: Computing Science and Statistics*, Research Triangle Park, NC, June.

1993 George W. Downs and David M. Rocke, "Strategies for Treaty Maintenance," Invited Presentation, *MIT/Harvard Joint Seminar Series on International Relations*, April.

1992 David M. Rocke, "Optimal Design for Calibration Problems in ELISA," Invited Presentation, *Mathematical Sciences Research Institute Symposium on Industrial Statistics*, Berkeley, May.

1992 David M. Rocke, "Statistical Design of Immunoassay Protocols," Invited Presentation, *American Chemical Society Annual Meeting*, San Francisco, April.

1989 David M. Rocke, "Robust Control Charts," Invited Presentation, Temple University, Philadelphia, PA, October.

1986 David M. Rocke, "Measuring Variation for Quality Improvement Applications," Invited Paper, *Annual Fall Technical Conference*, American Society for Quality Control, Charlotte, North Carolina.

1986 David M. Rocke, "Measuring Variations for Quality Control Applications," Invited Paper, *International Research Conference on Reliability and Quality*, Columbia, Missouri.

1985 David M. Rocke, "Robust Statistical Analysis of Interlaboratory Studies," Invited Paper, *1985 Gorden Research Conference on Statistics in Chemistry and Chemical Engineering.*

1984 David M. Rocke, "A Comparison of Robust and Standard Analyses of Interlaboratory Studies," Invited Paper, *Biometric Society ENAR meeting*, Orlando, Florida.

1982 George W. Downs and David M. Rocke, "Multivariate ARIMA Modeling and Municipal Finance," Invited Paper, *Conference on Applied Time Series Analysis of Economics Data*, sponsored by the American Statistical Association, U.S. Bureau of the Census and the National Bureau of Economic Research.

1979 David M. Rocke and George W. Downs, "Time Series with Episodic Disruptions," Invited Paper, *Second International Time Series Meetings*, October, Guernsey, U.K.

APPENDIX F

Dr. A. Dallas Wait
Curriculum Vitae

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AREAS OF EXPERTISE

Environmental chemistry, petroleum hydrocarbon chemistry, analytical chemistry, analytical method design and evaluation, sampling techniques and design, quality assurance, laboratory auditing, data usability and integrity, forensic chemistry, chemical fingerprinting, organic geochemistry, historical analytical chemistry practices, regulatory agency negotiations, laboratory and program management.

EDUCATION

Ph.D., Organic Chemistry, University of Rhode Island, 1980.
American Hoechst Chemical Graduate Fellowship.

B.S., Chemistry, University of Rhode Island, 1973.

PROFESSIONAL EXPERIENCE

1989 - Present — GRADIENT CORPORATION, Cambridge, MA
Principal. Environmental chemistry consulting practice includes evaluating the source and fate of chemicals in the environment, designing analytical chemistry methods and quality assurance programs, interpreting laboratory results, and determining the usability and integrity of data.

1986 - 1989 — ENSECO - ERCO LABORATORY, Cambridge, MA
Vice President and Technical Director. Responsible for providing senior program management and analytical chemistry program design services for various commercial and government clients involved with site investigations, waste characterization, and contaminant source identification.

1984 - 1985 — ERCO/A DIVISION OF ENSECO, Cambridge, MA
Vice President, Director of Analytical Services, and a cofounder of ENSECO. Responsible for the overall direction and management of organic, petroleum hydrocarbon fingerprinting, trace metal and wet chemistry laboratories, representing over 40 technical personnel. Involved also with activities associated with lab construction, public offerings (IPOs), laboratory acquisitions and mergers, and program management.

1978 - 1984 — ENERGY RESOURCES COMPANY, INC. (ERCO), Cambridge, MA
Director of Organic Chemistry Laboratory. Responsible for the management of the organic chemistry laboratory, consisting of gas chromatography and GC/MS facilities (utilized for solvent, petroleum hydrocarbon fingerprinting, pesticide, PCB, herbicide, priority pollutant, and specialty organic compound analyses). Business areas serviced include, in part, marine oil spill research, agency method development and evaluation studies, aquatic toxicology support, analysis of waste samples from alternative energy technologies (*e.g.*, fluidized bed combustion), product characterization, and priority pollutant analyses of wastewaters, drinking waters and site investigation samples, often for MGP sites.

PROFESSIONAL ACTIVITIES

- Expert testimony evaluating the integrity and usability of environmental chemistry measurements and sampling procedures, the source and fate of chemicals, and historical analytical chemistry practices.
- Member of the Editorial Board for *Journal of Soil and Sediment Contamination* (2002 – present).
- Recipient, representing Gradient, of the National Ground Water Association (NGWA) 2001 Outstanding Ground Water Project Remediation Award – Picillo Farm Site, Coventry, Rhode Island.
- Invited Member of the Scientific Advisory Board (SAB) for the International Conference on Contaminated Soils, Sediments and Water (2000-present).
- Invited Peer Reviewer for the *Journal of Soil and Sediment Contamination* (2000-2002). Papers critiqued generally involve analytical methods used to test for trace metal and organics in solid matrices.
- Member of MADEP MCP Data Quality Enhancement Workgroup – Overall Subcommittee (2000-present).
- Member of the Editorial Board for *Environmental Forensics* (1999 – present).
- Chairperson for *Risk and Risk-Based Decision Making* sessions of the 15th to 17th Annual International Conference on Contaminated Soils, Sediments and Water. UMASS-Amherst (October, 1999 to 2001).
- Member of the Test Method Coalition sponsored by Bergeson & Campbell, P.C. (1998-1999).
- Member of the Editorial Advisory Board for *Environmental Testing & Analysis* (1997 - 2001).
- Member of the Editorial Advisory Board for *Environmental Lab* (1991 - 1997).
- Participant in the course "Surface Analysis Techniques and Applications" relating to materials characterization applicable to forensic studies. Presented by Evans East, Princeton, NJ (September, 1998).
- Member of the Massachusetts Environmental Justice Network (1996 - present).
- Member of the Greater Boston Mass Spectrometry Discussion Group (1989-1993).
- Member of the environmental subcommittee for the Town of Princeton, MA (1989 - 1991).
- OSHA Health and Safety Training Course (in compliance with OSHA 1910.120 regulations), including initial 40 hour course and annual 8 hour refresher courses (1989 - present).
- Member of ASTM Committees developing guidance and standards for environmental sampling and analysis:
  - D34.02.10 Data Quality Objectives (1990 - 1991, 1993 - 1995) [Standard D5792]
  - D34.01.12 Heterogeneous Waste Sampling (1993 - 1996) [Standard D5956]
  - D34.02.04 Organic Analytical Methods (1994 - 1997) [various standards]
  - D34.02.13 Action Level Determination (1994 - 1998) [Standard D6661]
  - D34.01.03 Wipe Sampling for Organics (2000 - 2001) [Standard D6250]
- Contributing author to *Test Methods for Evaluating Solid Waste - Physical/Chemical Methods*, Second Edition, EPA-SW846 (1982).
- Participant in week-long sessions of the Organic Geochemistry Gordon Research Conference. Holderness, New Hampshire (August, 1974 and 1976).

PROFESSIONAL ASSOCIATIONS

American Chemical Society (ACS) • American Society for Testing and Materials (ASTM) • Boston Bar Association – Environmental Law Section (Adjunct) • Environmental Law Institute (Associate) • American Society of Forensic Geologists • Massachusetts LSP Association (Associate) • Society of Environmental Toxicology and Chemistry • International Society of Environmental Forensics

PROJECT LIST

Environmental and Forensic Chemistry Studies

Jellinek, Schwartz & Connolly (Washington, DC): Consulted on structural activity and aquatic chemistry issues (biodegradation, hydrolysis, photodegradation, fugacity) associated with coke ovens and tar refiners in support of the American Coke and Coal Chemicals Institute's (ACCCI) high production-volume (HPV) chemicals program.

Law Firm (Michigan): Provided expert testimony regarding potential sources of chlorinated and petroleum hydrocarbon contamination in groundwater, capillary fringe, and vadose zone soil samples at a Michigan site. Potential sources of contamination included, in part, gasoline stations, a dry cleaner, and a petroleum fuel pipeline.

PRP Group (Rhode Island): Conducted a forensic investigation to characterize a resin material uncovered at the Picillo Farm Superfund Site.

Law Firm (Texas): Provided expert testimony regarding the characterization of a petroleum hydrocarbon plume using GC/MS fingerprinting. Potential sources included, in part, natural gas condensates released from wellheads and pipelines, and refined gasoline.

Jellinek, Schwartz & Connolly (Washington, DC): Consulted on structural activity and aquatic chemistry issues (biodegradation, hydrolysis, photodegradation, fugacity) associated with petroleum additives and aliphatic esters in support of the Chemical Manufacturers Association's (CMA) high production-volume (HPV) chemicals program.

Petroleum Company (Oklahoma): Provided litigation support associated with hydrocarbon fingerprinting to determine the nature, extent and source of petroleum hydrocarbon contamination at a site in Louisiana. Potential sources included a jet fuel pipeline which supplies a nearby Air Force Base and a former petroleum refinery.

CBS-60 Minutes (New York): Designed and implemented an investigative sampling and analysis program to assess lead contamination of surficial soils in urban environments in the northeastern United States.

Petroleum Company (Pennsylvania): Conducted a forensic investigation (hydrocarbon fingerprinting and biomarker analysis) to decipher the source of a hydrocarbon sheen on the Allegheny River.

Law Firm (Georgia): Managed a large environmental investigation in response to a multi-party toxic tort, which involved evaluating chemical partitioning and plaintiff exposure pathways from a wood treating facility.

Law Firm (Massachusetts): Provided expert opinions utilizing petroleum hydrocarbon fingerprinting to discern the source of a domestic heating oil fuel spill in southeastern Massachusetts.

S.D. Warren (Maine): Designed and implemented an analytical chemistry research program evaluating the environmental impact of applying paper pulp waste to agricultural land. The study focused on the leachability of chlorinated phenols, resin acids, fatty acids, and volatile organics from soils.

Boston Edison Company (Massachusetts): Designed and implemented a sampling and analysis program to evaluate herbicide usage and contamination of soil and vegetation in power line right-of-way areas in Eastern Massachusetts. Herbicides evaluated included picloram, 2,4-D and 2,4,5-TP.

Power Company (Pennsylvania): Designed and implemented an analytical chemistry program to characterize and determine the source of foam occurring on the Susquehanna River.

University of Rhode Island: Conducted research at the RI Nuclear Science Center using neutron activation analysis to determine trace metal content of marine organisms in the Sargasso Sea (North Atlantic Ocean).

University of Rhode Island: Conducted research using hydrocarbon fingerprinting techniques to correlate sediment outcrop strata associated with notable archeological investigations conducted by Dr. Richard Leakey during the mid 1970s in the Lake Turkana (formerly Lake Rudolf) region of Kenya regarding the origins of humans.

Data Integrity Assessments

Law Firm (California): Provided expert testimony regarding perchlorate regulatory chemistry and data usability issues associated with a drinking water aquifer in southern California.

Law Firm (Louisiana): Developed and implemented a sampling and analysis program to evaluate the integrity of chemistry data previously produced in support of litigation associated with crude oil contamination originating from a pipeline.

Law Firm (Massachusetts): Provided expert testimony regarding the quality, usability and interpretation of testing data used to assess the source of historical fuel oil spills at an operating manufacturing facility.

Law Firm (California): Evaluated the integrity and usability of MTBE data obtained from a Los Angeles aquifer.

Law Firm (Illinois): Provided expert testimony regarding benzene measurement and representative sampling issues associated with petroleum refinery process wastewaters regulated under NESHAP (40 CFR Part 61, Subpart FF). Issues regarding fraudulent laboratory activities were significant in the case.

Law Firm (Massachusetts): Evaluated the quality, usability, and interpretation of fingerprinting data used to assess the source of historical petroleum spills at a bulk fuel terminal. The evaluation pertained to the applicability of insurance coverage for site clean-up activities.

Railroad (Delaware): Consulted on the applicability and implementation of PCB congener methods used in support of a NPDES wastewater discharge permit.

Law Firm (Massachusetts): Provided expert testimony regarding the interpretation and usability of PAH, volatile organic, petroleum hydrocarbon fingerprinting, and carbon (^{14}C) dating data used to discern potential sources of creosote, pine tar and petroleum constituents in soils at a site in Florida.

UniFirst Corporation (Massachusetts): Provided comments to U.S. EPA regarding the usability of analytical data used to derive proposed pretreatment standards for the industrial laundries point source category (40 CFR Part 441).

Petroleum Company (Oklahoma): Provided litigation support to determine the usability of indoor air data produced using TO-14 summa canisters in a residential area located over a former petroleum refinery in northwest Louisiana. Participated in numerous negotiation sessions with EPA Region VI regarding appropriate sampling and analysis methods for ambient air.

Law Firm (Michigan): Critiqued a series of arbitration expert reports pertaining to allocation of liability for contamination associated with antioxidant product tolling (specialty chemical manufacturing) and solvent reclamation processes at facilities sited on a former petroleum refinery.

U.S. Department of Justice (Washington, DC): Provided litigation support regarding the integrity of laboratory data produced in support of a NPDES wastewater discharge permit for a petroleum refinery in California.

Law Firm (Texas): Provided litigation support assessing the usability of fingerprinting data produced to differentiate incinerator sources of dioxin/furans (PCDD/Fs) in surface soils.

Law Firm (California): Provided litigation support evaluating the potential presence of MTBE in Los Angeles area groundwater and soils contaminated with gasoline.

Environmental Risk Services (Washington, DC): Evaluated the quality of data used by EPA to derive the pretreatment standards for the industrial laundries point source category. This work was supported by the Uniform and Textile Services Association (UTSA) and the Textile Rental Services Association (TRSA).

Law Firm (Arizona): Provided expert testimony regarding historical analytical chemistry and sampling practices for THMs and TCE in drinking water which municipalities should have been implementing during the early 1980s.

Petroleum Company (Oklahoma): Established and oversaw a sampling and analytical chemistry program to evaluate potential groundwater contamination from gasoline stations located in six states (WI, IL, IN, FL, PA,

MA). Testing included MTBE, EDB/EDC, and BTEX surveys, and petroleum hydrocarbon fingerprinting. Expert testimony was also provided regarding the use of the data for discerning contaminant liability.

Law Firms (Pennsylvania, New York): Provided expert testimony regarding the historical analytical chemistry capabilities of laboratories to analyze for TCE (and TCA) in groundwater and surface waters in the late 1960s.

Law Firm (California): Provided expert testimony regarding data quality issues associated mainly with PCB analyses for numerous site investigations at an operating manufacturing facility, and subsequently designed a new sampling and analysis program. Other chemicals of concern included petroleum hydrocarbons, solvents and metals. Provided opinions regarding the identification of PCBs (congener fingerprinting) for the purpose of source allocation, and designed novel wipe sampling procedures for porous surfaces to evaluate potential dermal uptake of PCBs. Participated in negotiations with California DTSC regarding data assessment and sampling strategies.

Law Firm (New York): Assessed the integrity of a sampling and analysis program designed to locate the sources of lead contamination in the drinking water system of a school campus located in New York.

Law Firm (Connecticut): Assessed data quality issues associated with leachate testing at the Beacon Heights Landfill in support of a tire manufacturer (Pirelli-Armstrong Rubber) involved with contaminant liability litigation.

Law Firm (Michigan): Provided expert testimony regarding the integrity of groundwater carbon tetrachloride data used for a site investigated by Michigan DNR.

Exxon (New Jersey): Participated in negotiations with New Jersey DEP regarding the usability of data relative to strict data validation results. The data was associated with a large remedial investigation at the Bayway Refinery, and successful negotiations resulted in saving Exxon significant resampling and reanalysis costs.

Law Firm (Washington, DC): Provided expert testimony for numerous toxic torts pertaining to the integrity of the analytical chemistry and sampling of the pesticide chlordane in residential settings.

Mining Company (Colorado): Assessed sampling procedures, data quality and data integrity, document control systems, and laboratory testing performance for site-specific chemicals and radionuclides in anticipation of litigation.

Law Firm (New York): Evaluated historical analytical chemistry practices used to monitor groundwater quality at an operating chemical company in New Jersey for the purpose of litigation.

Hazardous Waste Company (Ohio): Critiqued a RCRA Corrective Action Plan pertaining to data validity and usability, database management and risk assessment issues, and negotiated with EPA Region V and OEPA.

Law Firm (Pennsylvania): Provided litigation support to a pipeline company to assess the quality and usability of PCB data associated with numerous site investigations.

Data Quality Management

Malcolm Pirnie (New York): Consulted with EPA Region II and U.S. Army Corp. regarding appropriate test methods for delineating PCB "hot spots" in Upper Hudson River sediments.

Petroleum Refinery (Illinois): Established a laboratory contract program in support of benzene testing of process wastewaters for NESHAP regulatory compliance.

Arthur D. Little (Massachusetts): Managed a laboratory audit and performance evaluation program in support of the U.S. Army Assembled Chemical Weapons Assessment program at the Aberdeen Proving Ground, Maryland.

Petroleum Company (Louisiana): Designed and oversaw an analytical chemistry program for a RCRA closure of a 26-acre petroleum refinery sludge holding pond located in southwest Louisiana.

Chemical Company (New York): Provided QA oversight services for a RI/FS being conducted at an inactive chloralkali manufacturing facility. Contaminants of concern included mercury, PCBs, and solvents. The sampling and analysis program for mercury entailed low-level mercury and methyl mercury determinations using "clean-hands" sampling techniques.

Petroleum Company (California): Established and oversaw a national laboratory contract program during the mid 1990's in support of environmental investigations nationwide.

PRP Group (Rhode Island): Provided QA oversight services for monitoring and remediation activities at the Picillo Farm Superfund Site in Coventry, Rhode Island. One project involved "clean-hands" wastewater sampling and analysis for zinc and aluminum. Participated in numerous negotiations with EPA Region I regarding analytical method design, data interpretation, and data assessment procedures.

Petroleum Company (Oklahoma): Established and oversaw a national laboratory contract program during the early to mid 1990's in support of environmental investigations nationwide.

Raymark Industries (Connecticut): Provided quality assurance oversight for an RCRA facility investigation (RFI) at a former brake manufacturing facility contaminated with asbestos, lead, PCBs, solvents, and dioxin/furans (PCDD/Fs). Participated in numerous negotiation sessions with EPA Region I regarding analytical method design, salvaging historical data, data assessment, and interpreting data usability for human health risk assessment.

TAMS Engineering (New York): Designed a PCB congener analytical chemistry and sampling program, and oversaw the chemistry and quality assurance program to reassess the distribution of PCBs throughout a 200 mile stretch of the Hudson River ecosystem. Over 3,000 river water, sediment, particulate and biota samples were analyzed for PCB congeners during the program. Participated in negotiation sessions with EPA Region II regarding approval of an unique PCB congener analytical chemistry method and supporting data validation protocols.

Midwest Gas Company (Michigan): Evaluated laboratory performance associated with analytical testing for remedial investigations at Manufactured Gas Plant (MGP) sites.

Petroleum Company (Louisiana): Designed and oversaw an analytical chemistry program as part of a RI/FS at a former petroleum refinery site located in northwest Louisiana. Participated in numerous negotiation sessions with Louisiana DEQ and EPA Region VI regarding sampling and analysis methods.

Utility (New York): Performed confidential due diligence and auditing at eleven laboratories nationwide in consideration of an utility acquiring environmental laboratory businesses.

Anitec-International Paper (New York): Provided quality assurance oversight for a remedial investigation at an active photographic material manufacturing facility. Chemicals of concern included PAH hydrocarbons, solvents, PCBs and metals. Participated in numerous negotiation sessions with New York State DEC and New York State Department of Health regarding analytical methods, background measurements, and viable exposure pathways.

Petroleum Company (Louisiana): Conducted a series of laboratory audits of Louisiana-based labs to evaluate their ability to provide analytical services for site investigation and monitoring programs at a refinery in Lake Charles.

Utility (New York): Provided consulting services regarding business and logistical strategies to enter the commercial environmental laboratory business.

Argonne National Laboratory (Illinois): Provided quality assurance oversight for a remedial investigation at Air Force Plant 59 in Johnson City, New York. Test methods included field XRF analysis for certain trace metals (*e.g.* Pb, Cr, Cd). Negotiated with New York State DEC-Region 7 on behalf of the Air Force regarding chemicals of concern, detection limits and analytical methods.

Confidential Environmental Laboratory (New York): Provided consulting management services to upgrade operational and technical systems to meet New York State DEC requirements for environmental testing laboratories.

Stetson-Harza (New York): Provided quality assurance oversight for field sampling and chemistry services required as part of a RI/FS program at a landfill in Whitestown, New York. Supplemental court testimony was successfully provided to demonstrate data integrity.

Metcalf & Eddy (New York): Provided quality assurance services for numerous site investigations at inactive hazardous waste sites in New York, including corrective action for previous work conducted by other contractors. Negotiated directly with NYS DEC regarding the usability of data previously generated at some of the waste sites.

Exxon (Alaska): Participated in designing an analytical chemistry program, and oversaw analyses of sediment, water and swab samples collected in Prince William Sound following the *Exxon Valdez* oil spill. The program was intended to evaluate sources of petroleum hydrocarbons in the Sound, evaluate the progress of the oil spill cleanup, and evaluate ecological impacts.

Method Development/Assessment Programs

Confidential Utility (Northeast): Assisted in designing a unique sampling and analysis program in support of a research project to evaluate the possible emission of gases and chemicals resulting from faulting events occurring with underground power transmission lines encased in coal tar insulation.

U.S. Department of Justice (Washington, DC): Assisted in designing a storage stability study for malathion and malaoxon pesticides collected on air filters and alpha cellulose collectors associated with spray drift studies at a tropical fruit farm in Puerto Rico.

Womble & Carlyle (Georgia): Provided an expert report to OSHA critiquing a piezobalance method for analyzing respirable air particulates associated with a proposed OSHA regulation for indoor air.

U.S. EPA, Office of Research and Development (Ohio): Participated in a multilaboratory study to evaluate a GC/MS method for the analysis of PCB congeners and pesticides (Method 680).

Chemical Company (Ohio): Designed a negative ion chemical ionization mass spectrometry analytical chemistry program using, in part, isotope dilution methods for ultra low level analyses of the pesticides mirex and kepone in groundwater, soil, sediment, air (XAD-2), and tissue samples. Extensive negotiations with EPA Region V were necessary prior to method approval.

U.S. EPA, Quality Assurance Branch (Ohio): Managed a task order contract to validate six SDWA analytical chemistry methods proposed for trace level analysis of organics in drinking water, which focused on pesticides and volatile organic compounds.

U.S. EPA, Office of Solid Waste (Washington, DC): Managed task order assignments associated with the development/evaluation of analytical methods used to detect the presence of hazardous waste constituents and classify wastes. Several tasks included developing clean-up procedures for analyzing petroleum refinery wastes, conducting a nationwide waste oil characterization study, PAH analysis of coke wastes, and characterizing petroleum refinery wastes (*e.g.* oil/water separator emulsions, rag oils, still bottoms, slop oils) and paint wastes for delisting petitions. Also co-authored the 1982 second edition of SW-846 entitled "Test Methods for Evaluating Solid Waste," focused on GC and GC/MS methodologies.

Photographic Manufacturer (Massachusetts): Developed and oversaw a specialized GC monitoring program for polar organic solvents in various process wastestreams.

University of Rhode Island: Established a training program for university science departments to produce glass capillary GC columns for analytical chemistry research. The technology was developed under a tutelage visitation program at the Organic Geochemistry Unit of the University of Bristol, England, headed by Dr. Geoffrey Eglinton.

Product/Technology Assessments

Law Firm (Washington, DC): Evaluated the applicability and implementation of NSF extraction procedures to determine the leachability of lead from faucet systems regulated under California Proposition 65.

Law Firm (Washington, DC): Provided litigation support evaluating the chemistry of raw materials, intermediates, by-products and final products associated with waste generated in the manufacturing of the pesticide chlordane.

PRP Group (Michigan): Developed an analytical chemistry program and oversaw soil flushing experiments associated with evaluating remediation alternatives at the Demode Road site, located in Rose Township, Michigan.

Industrial Economics, Inc. (Massachusetts): Proposed testing methods to analyze for volatile organic compounds in consumer products. This project supported EPA studies being formulated to reduce tropospheric ozone levels.

U.S. EPA, Industrial Environmental Research Laboratory (North Carolina): Managed an analytical chemistry program designed to characterize aqueous, atmospheric and solid effluents generated from the combustion of various types of refuse derived fuels.

Arthur D. Little, Inc. (Massachusetts): Conducted an analytical chemistry program in support of a study to evaluate supercritical fluid extraction procedures for various materials, including hazardous waste.

Pennzoil Products Company (Texas): Oversaw a testing program during the mid-1980s to determine the PAH content of various motor oil products.

U.S. Printing Ink (New Jersey): Oversaw a testing program during the mid-1980s to determine the PAH content of various printing ink manufacturing intermediates.

Cabot Corporation (Massachusetts): Oversaw a testing program during the early 1980s to determine the PAH content of carbon black and manufacturing intermediates.

Major Newspaper (Massachusetts): Conducted a study in the early 1980s to determine the PCB content of marketplace bluefish.

UMASS Experiment Station (Massachusetts): Conducted a study in the early 1980s to determine the organophosphorus pesticide content of various cranberry foodstuffs.

Power Recovery Systems, Inc. (Massachusetts): Managed an analytical chemistry program designed to evaluate environmental contamination associated with fluidized-bed combustion technology. Compounds of interest included pyrogenic PAH hydrocarbons, PAH oxygenates, phenolics, and heterocycles.

Remediation Technologies, Inc. (Massachusetts): Managed an analytical chemistry program evaluating the presence of chlorinated dioxins/furans (PCDD/Fs), PAHs and pentachlorophenol generated by the incineration of creosote-contaminated soils collected from railroad facilities.

Tnemec (Missouri): Conducted leachate studies of coating materials used in water storage tank linings to assess the potential for solvent contamination into the water.

New York State Department of Environmental Conservation (NYSDEC): Oversaw an analytical testing program evaluating the effectiveness of remedial technologies being considered for the destruction of Love Canal wastes.

Bradford Soap Works (Rhode Island): Investigated rancid soap problems (anomalous fatty acid content) associated with raw materials used in manufacturing soaps.

Environmental Testing Programs

U.S. EPA, Effluent Guidelines Division (Washington, DC): Managed analytical chemistry service contracts involved with the screening of industrial wastewater effluents for priority pollutants. Managed another contract

which implemented isotope dilution GC/MS techniques for the analysis of organics in industrial wastewater samples.

U.S. EPA, Contract Laboratory Program (Washington, DC): Managed a series of analytical chemistry service contracts (for over eight years representing over 2.6 million dollars in revenue) in support of organic analytical services required for CERCLA Superfund site investigations.

U.S. EPA, Health Effects Research Laboratory (Ohio): Managed a large chemistry program analyzing purgeable organics in drinking water. Samples were analyzed in support of an epidemiological study correlating the presence of organic solvents in drinking water with increased incidence of certain types of cancer.

U.S. EPA, Region I (Massachusetts): Managed task order assignments (ten years) requiring analysis of environmental site and industrial waste samples for potential hazardous compounds.

U.S. EPA, Office of Water Regulations and Standards (Massachusetts): Managed an analytical chemistry program as part of the National Urban Runoff Program (NURP). In conjunction with the Massachusetts DEQE, analyses were performed for organic and trace metal priority pollutants in stormwater runoff from Lake Quinsigamond and the Mystic River Watersheds.

New York State Electric & Gas (New York): Managed a series of analytical chemistry programs evaluating soil contamination at Manufactured Gas Plant (MGP) sites throughout New York.

Union Camp (New Jersey): Managed numerous analytical chemistry programs in support of NPDES and site investigation programs for pulp and paper operations nationwide. Assisted in negotiations with the State of Virginia regarding Union Camp's wastewater disposal permit at the Franklin facility.

Real Estate Developer (Rhode Island): Oversaw an analytical chemistry program designed to characterize a former Manufactured Gas Plant (MGP) site in Newport, Rhode Island for the purpose of a real estate transaction.

Allied Chemical (New Jersey): Managed an analytical chemistry program in support of a multi-year ocean dumping permit in areas off the Northeast coast of the United States.

Numerous Municipalities (Northeast U.S.): Managed various analytical chemistry programs associated with SDWA drinking water regulations and potentially contaminated drinking water supply wells.

Numerous Industrial Corporations (Nationwide): Managed analytical chemistry programs required for NPDES permit applications. Also, managed projects involved with emergency spill response, waste disposal, and property acquisitions and transfers.

Numerous Engineering Firms (Nationwide): Managed various projects requiring analytical chemistry as part of site assessment, source liability, site cleanup, monitoring of closure activities, as well as for groundwater remediation.

New York State Department of Environmental Conservation (NYSDEC): Managed a series of contracts (for ten years representing over 1.8 million dollars in revenue) providing analytical services in support of remedial investigations, environmental enforcement, wastewater permitting, waste characterization (paints, oils, solvents) and municipal sludge land spreading studies. In addition, provided expert testimony in support of the analytical chemistry work performed under these contracts.

New York State Department of Law: Managed a series of analytical chemistry service contracts requiring chemical analysis of environmental and industrial waste samples in support of litigation.

U.S. Bureau of Land Management (Washington, DC): Managed an analytical chemistry program implementing petroleum hydrocarbon fingerprinting and polynuclear aromatic hydrocarbon distribution analyses to assess the ecological effects and fate of the Ixtoc oil spill in the marine environment of the Gulf of Mexico.

U.S. Geological Survey, Water Resource Division (Colorado): Managed a three-year contract providing analysis of organic compounds (volatile organics, semivolatile organics, and organochlorine and organophosphorus pesticides) in groundwater. The results were used to investigate the quality of the nation's water resources during the mid 1980s.

National Oceanic and Atmospheric Administration (Washington, DC): Oversaw tasks for an analytical chemistry program implementing petroleum hydrocarbon fingerprinting and polynuclear aromatic hydrocarbon distribution analyses to assess the ecological effects of the Amoco Cadiz oil spill off the coast of Brittany, France.

U.S. Bureau of Land Management (Washington, DC): Oversaw analytical chemistry work associated with establishing a petroleum hydrocarbon inventory for ocean sediments in the Georges Bank off the Northeast coast of the United States in anticipation of off-shore petroleum exploration drilling activities.

State of Maine Department of Environmental Protection: Managed task order assignments for analytical services required in support of environmental contamination investigations.

PUBLICATIONS

Wait, A.D. 2001. Environmental forensic chemistry and sound science in the courtroom. *Fordham Environmental Law Journal* 12: 293-327. Accessible on Westlaw and LEXIS.

Wait, A.D. 2000. Evolution of organic analytical methods in environmental forensic chemistry. *Environmental Forensics* 1: 37-46 (http://www.idealibrary.com on Ideal).

Brilis, G.M., Worthington, J.C. and A. D. Wait. 2000. Quality science in the courtroom: U.S. EPA data quality and peer review policies and procedures compared to the Daubert factors. *Environmental Forensics* 1: 197-203 (http://www.idealibrary.com on Ideal).

Wait, A.D. and L.L. Cook. 1999. Opportunities in environmental forensic chemistry analysis. *Environmental Testing and Analysis* 8(4): 31-32.

Wait, A.D. 1999. Evolution of organic analytical methods in environmental forensic chemistry. *International Journal of Environmental Forensics* 1(1): 68-86 (http://www.aehs.com/IJEF).

Wait, A.D. and E.L. Butler. 1999. Forensic chemistry: tools for discerning site liability. *Environmental Compliance & Litigation Strategy* 14(9): 4-5.

Wait, A.D. 1999. Non-petroleum forensic chemistry. *Trends in Risk & Remediation* 16: 4-5 (Fall, 1999).

Slayton, T.M., Valberg, P.A. and A.D. Wait. 1998. Estimating dermal transfer from PCB-contaminated porous surfaces. *Chemosphere* 36(14): 3003-3014.

Butler, E.L., Frisbie, S.H., Schabron, J.F., Sorini, S.S. and A.D. Wait. 1997. New ASTM TPH Screening Method. *Environmental Lab* 9(1): 11-14.

Wait, A.D. and L.L. Cook. 1997. Analytical issues for Persistent Organic Compounds. *Trends in Risk & Remediation* 5: 5-6 (Winter, 1997).

Chapnick, S.D., Sharma, M. and A.D. Wait. 1996. Misuse of TCLP methods. *Environmental Lab* 8(1): 22-25.

Wait, A.D., and G.S. Douglas. 1995. QA for nonstandard analytical methods. *Environmental Lab* 7(6): 30-34.

Wallin, B.K., E.J. Hamilton, and A.D. Wait. 1994. Minimizing data quality liability. *Environmental Lab* 6(4): 19-22.

Wait, A.D. and T.S. Bowers. 1993. The intrinsic value of nondetects. *Environmental Lab* 5(1): 20-23.

Sauter, A. and A.D. Wait. 1992. Perspectives on data integrity and quality. *Environmental Lab* 4(3): 25-33.

Maney, J.P. and A.D. Wait. 1991. The importance of measurement integrity. *Environmental Lab* 3(5): 20-25.

Chrostowski, J., A.D. Wait, E. Kwong, and A. Jefferies. 1985. "Assessment of Organic Contaminants in Emissions from Refuse-Derived Fuel Combustion." EPA Report No. EPA/600/2-85/155.

Boehm, P.D., A.D. Wait, D.L. Fiest, and D. Pilson. 1982. "Ixtoc Oil Spill Assessment: Chemical Assessment-Hydrocarbon Analyses." Final Report, Bureau of Land Management (BLM) Contract No. AA851-CTO-71.

Wait, A.D. and P. Abell. 1982. N-Alkane and fatty acid stratigraphy of the Lake Turkana Basin, Kenya. *Organic Geochemistry* 4: 37-50.

Wait, A.D., *et al.* 1982. Contributing author to *Test Methods for Evaluating Solid Waste - Physical/Chemical Methods*. Second Edition. Office of Solid Waste, EPA SW-846.

Wait, A.D., E. Kwong, A. Jefferies, C. Rodgers, and N. Moseman. 1982. "Assessment of Organic Contaminants in Emissions from Refuse-Derived Fuel Combustion." Final Report, EPA Contract No. 68-03-2771.

Perry, G., E. Silvestro, and A.D. Wait. 1980. "An Investigation into Herbicide Usage on Boston Edison Right-of-Way #4 in Weymouth, Massachusetts." Special published report for Boston Edison Company.

Wait, A.D. 1979. *Organic Molecular Stratigraphy of the Lake Turkana Basin, Kenya.* Ph.D. Dissertation, University of Rhode Island.

PRESENTATIONS

Wait, A.D. 2001. Chaired "*Risk & Risk-Based Decision Making* session at the 17th Annual International Conference on Contaminated Soils, Sediments and Water." UMASS-Amherst. October 25, 2001. Amherst, Massachusetts.

Butler, E.L., A.D. Wait, G. Douglas and J. Brown. 2001. "Tiered Analytical Approach is a Versatile and Cost Effective Tool in Answering Forensic Questions." Poster presented at the First International Congress on Petroleum Contaminated Soils, Sediments & Water. April 16, 2001, Imperial College, London, England.

Wait, A.D. 2001. "Producing Defensible Pesticide Data." Presented at the NYSDEC workshop Defensible Investigation & Sampling Techniques for the Pesticide Control Specialist, April 24-26, 2001, Albany, New York.

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APPENDIX G

W. Marcus Cooke
Comments

Peer Review Comments on "Technical Support Document of Detection and Quantitation Regulations under the Clean Water Act" Pursuant to EPA Contract No. 68-C-98-189, Under Subcontract Task Order No. 3-49 from Versar Inc., to Marcus Cooke

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The U.S. Environmental Protection Agency (EPA) developed Method 1631B for determination of mercury (Hg) "in the range of 0.5–100 ng/L"[1]. EPA Method 1631B has a broad range of applications. "The Method is based on a contractor-developed method (Reference 1) and on peer-reviewed, published procedures for the determination of mercury in aqueous samples, ranging from sea water to sewage effluents[2–6]."

The method detection limit (MDL) using procedures described in 40 CFR 136, Appendix B was stated in Method 1631B to be 0.2 ng/L when no interferences are present. The minimum level of quantitation (ML) was stated as having been established at 0.5 ng/L. Method 1631B states that MDLs as low as 0.05 ng/L can be achieved for low Hg samples by "using a larger sample volume, a lower BrCl level (0.2%), and extra caution in sample handling". EPA has published a number of guidance documents and training materials to assist in clean sampling and sample handling with Method 1631.

Method 1631B further states that detection limit and minimum levels of quantitation usually are "dependent on the level of interferences rather than instrumental limitations".

Although Method 1631B is cited as a "performance-based method", equivalency must be met. In fact Method 1631B states that any modification of this Method, beyond those expressly permitted, "shall be considered as a major modification subject to application and approval of alternate test procedures under 40 CFR 136.4 and 136.5". Thus the detailed methodology, sampling, sample handling, and Quality Control techniques described in Method 1631B will be rigidly followed by any group regulated under the National Toxics Rule, the Great Lakes Water Quality Initiative, or National Pollutant Discharge Elimination System (NPDES) permitting under the Clean Water Act. As such it is important to provide technically accurate, efficient, and laboratory-friendly guidance for any group attempting to generate defensible data using Method 1631B or any of the EPA Office of Water approved methods used in the aforementioned regulations.

This document was prepared in response to the "Charge to Reviewers" working under a subcontract to Versar Incorporated to provide a peer review for Method 1631B [7] as described in "Technical Support Document for the Assessment of Detection and Quantitation Concepts". "Charge to Reviewers" does not cite Method 1631, Revision C,

which is dated March 2001 in the pertinent method document, and modifies test method sections 12.4.2 and 9.4.3.3 to clarify use and reporting of field blanks[8]. This document refers only to a review of EPA Method 1631B, not modifications made through EPA Method 1631C.

Responses to Questions for Peer Reviewers

Question 1. *In Chapter 2, EPA recognizes and is willing to accept other detection and quantitation concepts, and has attempted to identify concepts that have been widely used or are widely known. Are there other concepts and procedures that EPA should evaluate? If so, please provide supporting rational and citations.*

In recent years budgetary constraints have limited EPA's ability to perform the extensive validation studies conducted in the 1980s on earlier methods like MCAWW and "600 Series" methods. While monies were constrained, legal and technical drivers moved ahead unabated:

- Improved method measurement techniques (*e.g.*, atomic fluorescence for Hg)
- New laws and regulations requiring more analytes and lower levels (*e.g.*, The Biosolids Rule)
- Advances in basic knowledge, especially risk-related effects (*e.g.*, the EPA Dioxin Reassessment)

Alternate Approaches Could Include a Body of Method Verification at Low Concentration Detection Performed in Europe -

EPA could consider data reliability and detection approaches that have been developed by the European Union (EU). For a long time EPA methods have been considered the "gold standard" in much of the world. In recent years the EU has been using and extending basic EPA methods, especially in the area of operational quality control.

One example is EPA Method 1613b, a method used globally to measure dioxin and furan using high-resolution mass spectrometry (HRMS) in many matrices, not just Clean Water Act samples for which the method was developed. On July 1, 2002, the EU implemented comprehensive regulation of human food and animal feed using the operational equivalent of Method 1613b. Vegetable foodstuffs as an example must be tested at levels below 0.3 pg/g (parts per trillion) Toxic Equivalence Quotient (TEQ).

Chapters 2 and 3 address the issue of international and risk-based regulations successfully operating below the method-defined MDL (Chapter 3, Page 3-5). Method 1613b lists

compound ML at 1-5 pptr in solid samples which corresponds to an order of magnitude higher detection than the official food/feed dioxin limits imposed in Europe.

When U.S. TEQ reporting protocols were applied in Europe, Method 1613b could not be used due to quality control issues, not detection issues. Since non-detected analytes are reported as zero values in the U.S., many American laboratories report erroneous results. All non-detects are reported as zero so no correction for detection is made to Method 1613b data for environmental reporting. The U.S. Food and Drug Administration (FDA) does report non-detects, using 1/2 the MDL in dioxin/furan computations that involve TEQ for regulatory purposes.

EU regulators applied an Upper Bound reporting limit where all non-detects are found, using the EPA Method Detection Limit (MDL) for each analyte. This forces laboratories to achieve levels available with modern instrumentation, otherwise the Upper Bound reporting level is above the regulatory compliance level and the data (or foodstuffs) are rejected.

Also many European Union (EU) procedures have trueness criteria. This is accuracy determined by percent (%) recovery of an accepted reference material. Trueness is a valuable improvement to EPA methods and will be discussed later. In order to incorporate trueness into an EPA method validation study, an appropriate reference material would need to be developed ahead of time and included in validation studies.

Eppe and Pauw have detailed the elements of uncertainty that affect detection limits and uncertainty in ultra trace dioxin/furan measurements [9-11]. Statistical evaluation of detection and data reliability for these data is based on ISO 17025 requirements. ISO 17025 includes laboratory-specific uncertainty estimation as a part of data validation. Analytical chemists have to demonstrate the quality of their measurements by associating the evaluation of uncertainty with their results.

This data treatment is based on a Eurachem Guide, which provides guidelines to evaluate uncertainty in analytical measurement [12].

Also recent VAM protocols give additional tools for uncertainty evaluation from validation data. The ISO/VAM process to evaluate uncertainty is based on 4 stages:

- First - Specify the measurand.
- Second - Identify uncertainty sources.
- Third - Quantify uncertainty components.
- Fourth - Calculate combined or total uncertainty.

Figure 1 shows a cause and effect diagram presented by Eppe *et al.* to show components of detection and uncertainty in analytical measurements. The strength of this treatment is a tested system to rigorously measure individual elements of data uncertainty and detection.

Eppe *et al.* [9] were able to sum individual analytical parameters and quantify principal sources of uncertainty for ultra trace measurement of dioxin/furan in food products as shown in Figure 2.

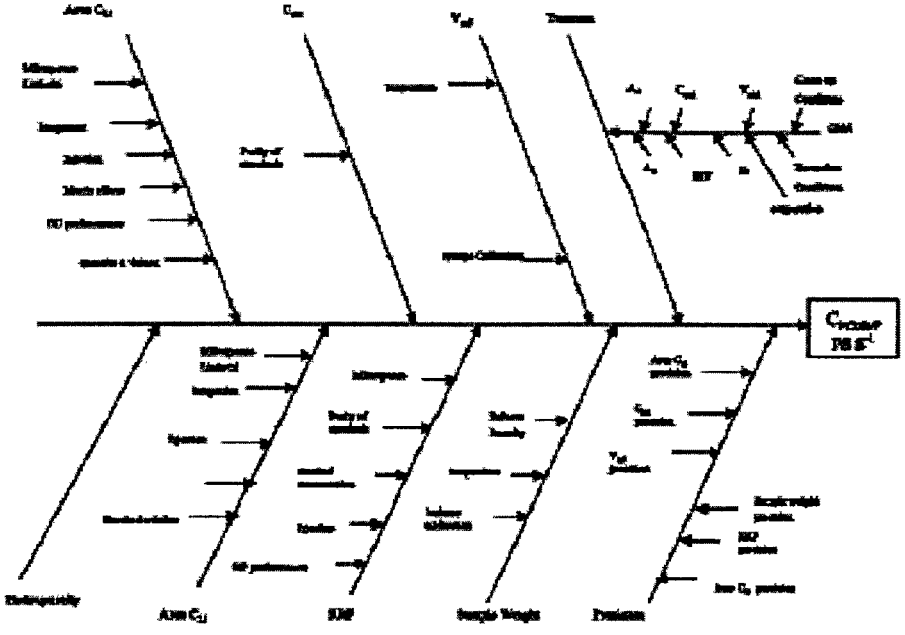

Figure 1. Cause and Effect Chart for Uncertainty and Detection in Analytical Measurements from Eppe *et al.* [9].

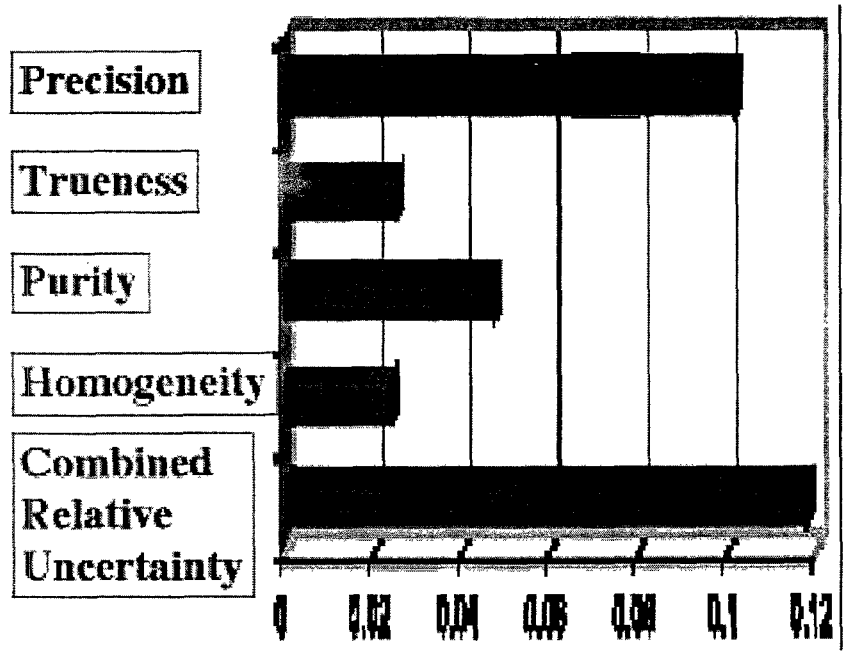

Figure 2. Contribution to the Measurement Uncertainty for Dioxin/Furan Analysis in Food and Feed from Eppe *et al.*[9].

EPA may want to consider recent advances in the statistical treatment of analytical method data that has evolved in Europe for three reasons.

- The EU is conducting the second largest trace chemical analytical program in the world. EU testing will exceed $1B in the first three years. (EPA is the record holder with the Contract Laboratory Program, $1.5B+).
- The EU has applied an EPA 1600 method equivalent (1613b) to a regulatory program that screens all food and animal feed used, produced or imported into Europe.
- The subject EU program has developed practical solutions to applying modern ultra trace measurements (and statistical verification) to a legally-based, widely-applied testing program.

Peer Review Comments - TSD Detection and Quantification

Question 2. *In Chapter 3, has EPA adequately identified and characterized the issues that need to be considered when evaluating detection and quantitation limit concepts in the context of implementation under the Clean Water Act? If not, please identify additional issues and provide a rationale for each addition. Are there any issues discussed that are not critical and can be detected? If so, please identify those issues and provide a rationale for each deletion.*

In Chapter 3 the TSD has done a good job of identifying technical issues that affect data quality and subject legal-regulatory constraints under which the Agency is operating (specifically CWA and NTTA).

Chapter 3 states six (6) specific issues EPA is charged with evaluating as part of a court-directed settlement:

1. Statistical model selection criteria,
2. Parameter estimation,
3. Statistical tolerance and prediction,
4. Challenge study design criteria including measurement levels,
5. Interlaboratory effects,
6. Probability design.

The TSD lists twenty (20) technical/regulatory issues that should be considered in implementing this effort. These issues can be grouped into 5 (five) categories: A. Method Performance Criteria; B. Laboratory Performance and Method Flexibility; C. Regulatory Constraints; and, D. Quality Control

TABLE I. 20 TECHNICAL/REGULATORY TOPICS ADDRESSED IN THE TSD

A. Method Performance Criteria

1. Ease of Use
2. Background
3. Instrument Non-Response
4. Lower Limit of Measurement
5. Matrix Effects
6. Outliers
7. Sources of Variance

TABLE I. 20 TECHNICAL/REGULATORY TOPICS ADDRESSED IN THE TSD
(Continued)

B. Laboratory Performance and Method Flexibility

8. Descriptive vs. Prescriptive Use of Lower Limits of Measurement
9. Laboratory Performance Verification
10. Laboratory-Specific Applications
11. Non-Regulatory Applications

C. Regulatory Constraints

12. Cost
13. False Positives/Negatives
14. Method Development
15. National vs. Local Standards of Measurement
16. NPDES Uses
17. Use of Pairs of Procedures
18. Voluntary Consensus Body (VCB) Procedures

D. Quality Control

19. Censoring Data
20. Degradation of Method Performance Over Time

Chapter 3 addresses most of the twenty (20) technical elements. Also the TSD addresses elements of the six (6) directed issues. Actual implementation of these technical and statistical issues would require a careful study that either controls or evaluates the effect of each directed issue (or technical issue) of concern. EPA may want to consider some additional issues which may have a significant effect on the reliability of data produced at ultra trace levels, whether to determine the initial presence of an analyte like mercury, or reliably apply regulations at a discharge limit.

General Comment on Quality Control and the Use of Reference Materials -

The technical issues in Chapter 3 concentrate on method and regulatory issues and give less attention to Quality Control. Quality Control should be considered in greater depth.

Peer Review Comments - TSD Detection and Quantification

As mentioned earlier, Method 1631B identifies interferences rather than instrumental limitations has having the greatest negative effect on detection limits and minimum quantification levels. The TSD discusses use of real world matrices in determining detection or quantitation limits at low levels (*cf.*, page 3-4). Operational laboratory performance can be addressed by use of appropriate reference materials that demonstrate the ability to handle interferences and low level detection as an operational quality control procedure.

Calibration required in Method 1631B could be enhanced by use of a reference material which contains a "real world" matrix, and also mercury forms known to exist in natural samples. Method 1631B states: "The Method is based on a contractor-developed method (Reference 1) and on peer-reviewed, published procedures for the determination of mercury in aqueous samples, ranging from seawater to sewage effluent (References 2–5)." As such Method 1613B is designed for samples ranging from reagent water to saline samples, and samples with high dissolved matter contents.

Method 1613B further defines mercury forms amenable to this technique: "Total mercury—all BrCl-oxidizable mercury forms and species found in an unfiltered aqueous solution. This includes, but is not limited to, Hg (II), Hg (0), strongly organo-complexed Hg (II) compounds, adsorbed particulate Hg, and several tested covalently bound organo-mercurials (*e.g.*, CH3HgCl, $(CH_3)_2Hg$, and $C_6H_5HgOOCCH_3$)."

Elemental mercury in nature often converts to Cinnabar or meta-Cinnabar, forms of mercuric sulfide. These are very stable, innocuous forms of mercury. Ambient samples can also contain organomercurials that have elevated human toxicity.

EPA might consider a demonstration study to show how "safe" and "unsafe" mercury forms are oxidized by BrCl, and are subsequently measured by this method, especially at low concentrations near the limit of detection.

An appropriate reference standard could be developed that incorporates the designated sample types (e.g., sewerage sludge, brackish and saline waters), challenge concentration ranges, and mercury forms described in Method 1631B.

For example a reference standard based on saline sewage effluent, spiked with known amounts of cinnabar, elemental mercury, and mercury salts could be developed to challenge laboratory performance over the full range of intended applications. (Organomercurials may be problematic in such a standard due to safety and secondary calibration limitations.). Such a standard could be used to measure trueness, and to eliminate data from laboratories that can not procedurally handle complex environmental samples.

Comment on Technical Issues - A. Method Performance Criteria

Ease of Use -

The complex theoretical treatments defined in this TSD and resultant additional analyses required in regulatory applications of Method 1631B may produce significant cost due to new supporting analyses needed to demonstrate detection and data reliability. The TSD does not address cost to users, but consideration of ease-of-use and cost should be included in any final revisions arising from this process.

Background, Matrix Effects, Sources of Variance -

The TSD gives considerable discussion to the problems that arise from background, matrix effects and sources of variance. Other topics like instrument maintenance, reliability and time stability of calibration standards, anion solubility effects, and related topics are also important to implementation of the method. EPA has done a good job addressing these issues, both in the TSD and in Method 1631B.

Instrument Non-Response, Lower Limit of Measurement, Outliers -

The TSD spends considerable time addressing models to define limit of detection. Also instrument non-response is discussed in detail.

Good quality control would include control charts that identify statistically significant loss of response at the MDL or alternate minimum detection level. This discussion does point out the operational difficulty in applying a method-defined MDL to single-laboratory determinations of few samples.

Peer Review Comments - TSD Detection and Quantification

Data in the TSD and referenced publications cite the loss of precision for ultra trace determinations near the limit of detection. Eppe *et al.* [10] plotted this effect as shown in Figure 3.

The subject of outliers was given limited attention in Chapter 3. Outlier treatment is a statistically valid area of data treatment. Cochran's test, and single/double Grubb's tests are useful in evaluating interlaboratory data sets to determine outliers and stragglers. Other classical outlier tests could also be evaluated in examining the data sets used in the TSD.

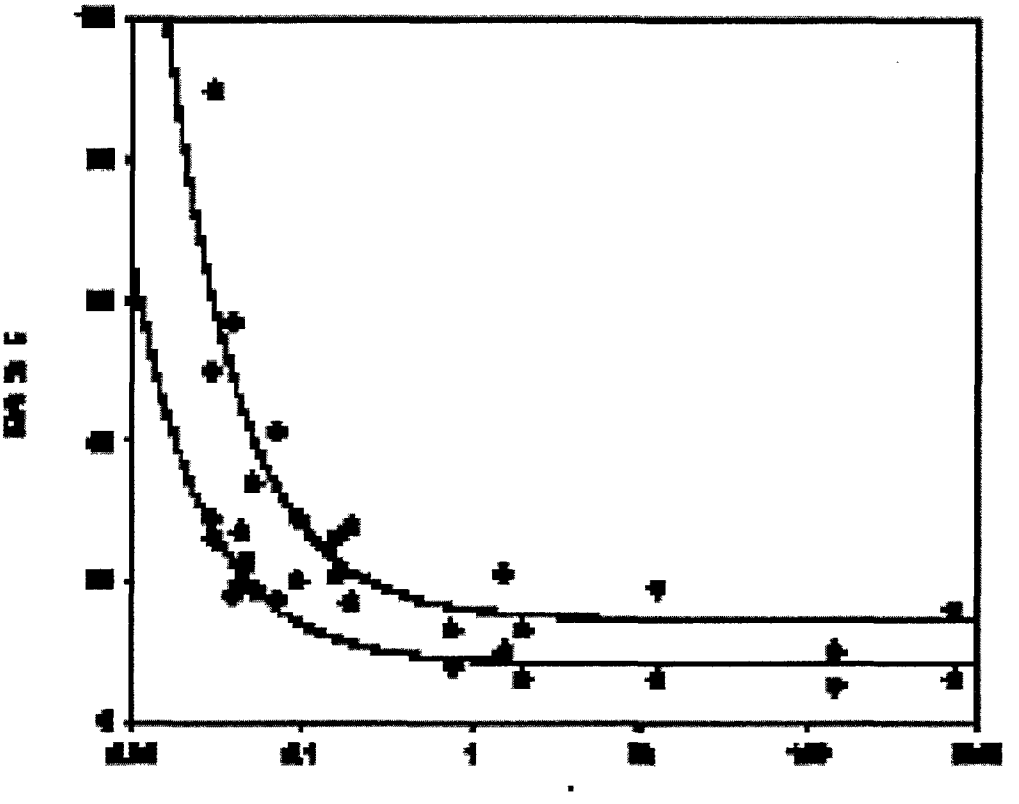

Figure 3. Coefficient of Variance *Versus* Concentration for Feed Samples at Parts-per-Trillion Levels Using an EPA Method 1613b Equivalent Procedure.

Comment on Technical Issues - B. Laboratory Performance and Method Flexibility

Descriptive vs. Prescriptive Use of Lower Limits of Measurement -

EPA typically walks a thin line in defining descriptive versus prescriptive procedures. Regulatory requirements built into EPA "Final Rules" are very difficult to change and cause a high level of legal liability to laboratories and data users. It is important for EPA to build as much flexibility as possible into CWA methods in order to prevent "locking" unreasonable or unsound procedures into Final Rule methods.

Laboratory Performance Verification, Laboratory-Specific Applications, Non-Regulatory Applications -

Laboratory performance is built into Method 1631B, however quality control procedures could be strengthened to insure adequate day-to-day demonstration of laboratory performance. This issue is discussed several times in this review.

Non-Regulatory Applications require individual treatment. Uses like risk assessment, screening, product of process monitoring, CERCLA surveying, all are valid applications of EPA numbered methods, but all require specific method modifications that are often beyond the scope of a method defined for a specific matrix or regulatory application (*e.g.*, Method 1631B for CWA compliance). In practice most 1600 series methods are used for many applications beyond their original intention. Typically the user must make and defend EPA method modifications applied to new analytes or new matrices.

Comment on Technical Issues - C. Regulatory Constraints

Method Development, False Positives/Negatives, Cost -

Chapter 3, and other parts of the TSD, spent a lot of effort reviewing method development and the topic of false positives and false negatives. Obviously the risk of a false negative must be thoroughly addressed in any health-protective regulatory environmental method. Likewise false positives cause unnecessary disruption to the regulated community. EPA is correct in giving this topic significant consideration.

Cost was not addressed adequately in the TSD; however, finalization of this review process and proposed method modifications would need to be identified before cost could be estimated. Method modifications could lead to very expensive monitoring programs

for the regulated community and responsible regulators. This topic should be fully addressed in summary reviews of this TSD.

National vs. Local Standards of Measurement, and NPDES Uses -

By law local restrictions must be equally stringent (or greater) than Federal rules. This process is addressed in current law. Also NPDES permitting is well established in the United States. I am not aware of any unusual legal or procedural difficulties that arise from a review of this TSD.

Use of Pairs of Procedures -

EPA has stated in the TSD that one primary procedure is needed for clarity and to avoid confusion among stakeholders. If alternate procedures are needed, the EPA Clean Air Act system of reference and equivalent methods has worked well, and could be a model for EPA to follow under the Clean Water Act.

Voluntary Consensus Body (VCB) Procedures -

EPA has strived to include VCB methods in the TSD and has conducted an extensive review and discussion of candidate VSB procedures. This author only suggests including international VSBs (especially European NGOs) due to extensive recent investigations of detection and quantification issues on similar species.

Comment on Technical Issues - D. Quality Control

Censoring Data, Degradation of Method Performance Over Time -

Method flexibility is discussed in the TSD and considers time-dependent modifications to rigid methods. EPA is gaining experience in this area and newer methods do address this concern. EPA has developed an evolving method development process, which has been shown to be responsive to this issue.

Peer Review Comments - TSD Detection and Quantification

Question 3. *Do the evaluation criteria in Chapter 4 adequately reflect the discussion of issues identified in Chapter 3? If not, please explain. Do you believe EPA should eliminate any of the six evaluation criteria or add other criteria? If yes, please identify the criteria to be added or eliminated and explain your rationale.*

Six (6) criteria are addressed in Chapter 4:

Criterion 1. Scientific Validity
Criterion 2. Demonstrated Method Performance
Criterion 3. Single Laboratory Method Practical, Affordable Procedures
Criterion 4. Assure 99% Detection Confidence in an Experienced Laboratory
Criterion 5. Assure Reliable Quantification Limit in an Experienced Laboratory
Criterion 6. Procedures are Responsive to the Clean Water Act

Scientific validity is defined two ways: legal reliability and scientific practice. Criterion 1 is defined by U.S. Supreme Court decisions defining expert testimony. Scientific validity is based on publication in the open literature, competent peer review, and general acceptance in the scientific community.

The legal basis for Criterion 1 as stated in the TSD is as follows:

1. Procedure which can and has been tested.
2. Publication and peer review.
3. Known or estimable error rate.
4. Standards to control operation.
5. Widespread acceptance in the scientific community.

The primary procedures evaluated by EPA for detection and quantification appear to meet most of these conditions, *e.g.,* MDL/ML, ATM IDE, ACS LOD, IUPAC/ISO Detection Limit. One open question concerns condition 4, "Standards". The TSD interprets this condition to mean well-documented methodology. U.S. Constitutional law intended metrology, the legal recognition of reference measures, as a Federal responsibility. If the court's intent was to include legal measures (metrology) as part of expert testimonial evidence, then the need for a defined reference material, or EPA audit standard, is implied in Criterion 1 and should be considered. This reviewer is not competent to answer this legal question. All the other elements of Criterion 1 seemed to be addressed in the subject TSD.

Criterion 2 appears to be met under EPA Method 1631B and other EPA-cited methods used as examples in the TSD. Measurement of variability and defined method expectations may require a special study that addresses all candidate alternate procedures and parameters that interested stake holders deem significant.

Peer Review Comments - TSD Detection and Quantification

Criterion 3 addresses performance of a procedure used by a single laboratory that is practical and affordable. This criterion is important because it isolates theoretical estimators, and large demonstration studies (interlaboratory and intralaboratory comparisons), from the fundamental application of any EPA method for single or small numbers of determinations. The most common situation is a laboratory performing many types of analysis but must peform EPA Method 1631B on a periodic basis where reproducibility is poor.

Criterion 3 should judge method ruggedness and appropriate quality control tot make a method reliable as well as "laboratory friendly". Criterion 3 addresses cost which is very important but this may need to be a final estimator after other parameters are settled.

Criteria 4 and 5 address the primary subject matter of the TSD detectability (Criterion 4), and quantifiability (Criterion 5). As such they are significant and should be maintained.

Criteria 6 addresses conditions in the method that meet Federal limits and allow for more stringent application by local regulatory bodies. This Criterion is essential and can not be changed.

These six criteria should provide a vigorous review of the conditions set out in the TSD. This reviewer feels that Criterion 3 should be strengthened both in performance discussions and proposed method modifications. Single laboratories, working independently "start from scratch" each time they perform the method. Quality control should be sufficient to insure reliability in single, isolated determinations of small sample sets, as well as large commercial laboratories performing many tests.

Peer Review Comments - TSD Detection and Quantification

Question 4. *Is the assessment in Chapter 5 of the TSD valid? Are the detection/quantitation concepts presented in the that (sic) chapter conceptually and operationally sound? Identify positive and negative features and justifications for your conclusions.*

The assessments given in Chapter 5 address the six evaluation criteria. As stated before, the challenge techniques seem to have a common limitation, procedural verification. Either the technique does not have a defined procedure to determine statistically rigorous measures of performance, or those measures are not available to adequately compare with EPA's MDL and ML.

MDL and ML have stood the test of time and provide a proven methodology which meets defined evaluation criteria stated in the TSD.

The Chapter 5 assessment appears valid based on stated criteria. Detection using MDL, in my opinion, is valid. Quantification concepts are subject to a higher degree of scientific challenge and interpretation.

Evaluation criteria stated in Chapters 3 and 4 do not address adequate measures to estimate increased variability near the limit of detection. Nor do they establish rigorous criteria for data acceptance. In practical laboratory operations techniques like control charts, maintained over time, would provide reliable measures of variability during actual laboratory operation.

The review process might be strengthened if EPA were to suggest experiments to evaluate alternate detection-quantitation procedures.

Operational procedures (control charts, reference standards, audit standards) would provide additional confidence in method performance at ultra trace levels in "real world" samples.

Peer Review Comments - TSD Detection and Quantification

Question 5. *Do you agree with the conclusions presented in Chapter 6? If not, please explain.*

I agree with EPA's primary conclusions as stated in Chapter 6, based on the conditions laid out in Chapters 3, 4 and 5. Furthermore EPA has documented that Method Detection Limit (MDL) is a sound estimator of initial signal response in a broad range of analytical methods. MDL has stood the "test of time" and I could not find a convincing statistical argument to replace MDL. However alternate methods do demonstrate potential improvements to MDL implementation (*e.g.*, criteria for initial spike determination and selection). ML and other candiate procedures for quantitation limts show significant variability.

An overall conclusion from reading the TSD is that EPA has made a strong case for maintaining MDL and ML as reference procedures. Alternate procedures could be accepted if formal acceptance criteria were developed and agreed by all parties. Then side-by-side testing would be needed to evaluate strengths of candidate procedures, and adherence to acceptance criteria.

There are no strong arguments in the TSD that would cause a level of concern needed to suspend EPA regulatory programs or methodology pending additional review. However there is evidence for additional study of variability near method detection. Figure 3 above, and comparison data in Appendix B for mercury illustrate this point. Two equivalent validation programs were plotted in Appendix B, EPA and AAMA. AAMA data for mercury by ICP/AES (Method 200.7) are shown in Figure 4. EPA data for mercury by ICP/AES (Method 200.7) are shown in Figure 5. Both plots show response versus concentration for known standards. EPA data are plotted on a logarithmic scale which tends to spread observed values. All three plots show that low level samples are subject to higher relative variance and should be treated differently from data above an agreed quantitation (or quantification) limit.

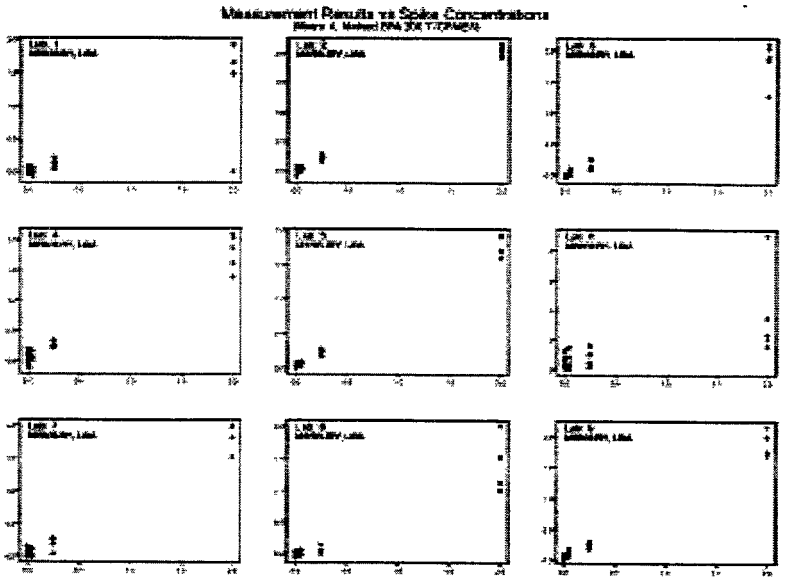

Figure 4. Method 200.7 Data for Mercury Response versus Concentration, AAMA Data from Six Laboratories.

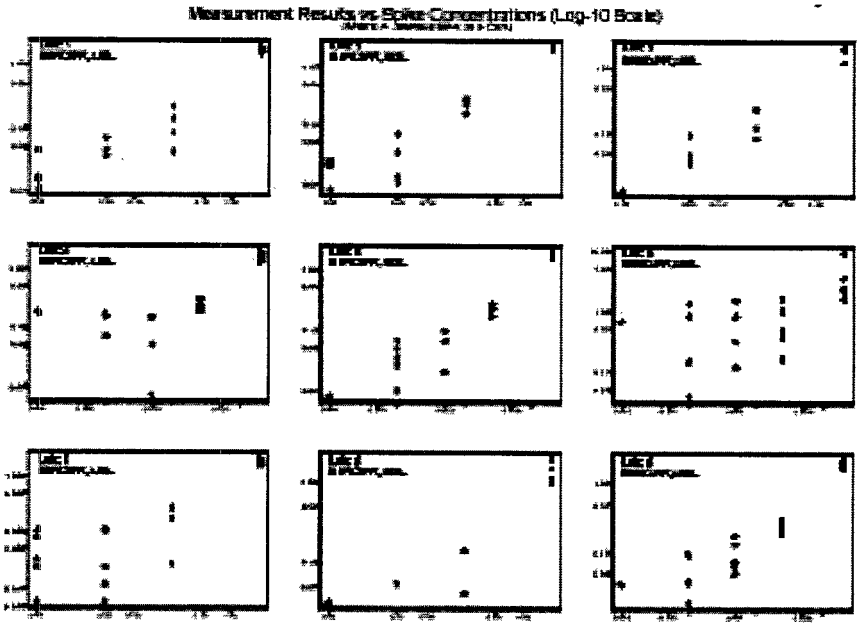

Table 5. Method 200.7 Data for Mercury Response versus Concentration, EPA Data from Six Laboratories, Log_{10} Plot.

Peer Review Comments - TSD Detection and Quantification

Question 6. *Prior to proposal of revised detection and quantitation concepts, should EPA evaluate other available data sets? Bearing in mind that in order to effectively assess various concepts, data sets must reflect measurements made below the detection limit, in the rang o detection and quantitation limits, and in the normal measurement range of the method, are there any available data sets that you recommend EPA consider? If so, please identify them and explain why they are appropriate.*

I am not aware of any specific data sets that could elucidate the various approaches and challenges listed in the TSD. Even if such databases exist, it would be very difficult to make the appropriate computations and solicit adequate reviews from interested parties given the limitations of the six evaluation criteria.

EPA has identified several candidate detection-quantification models that challenge the basic MDL and ML measures used in many EPA water-based analytical procedures. Most of these systems have not had method validation performed with the rigor EPA requires for legally defensible data. For example in Chapter 5 ("Assessment") four of the candidate alternate procedures: ACS (LOD), IUPAC/ISO (CRV), and IUPAC/ISO (MDV) fail due to the "absence of a procedure" for determining the value of interest. ASTM (IDE) is rejected for a number of reasons.

Most of these procedures are rejected because they have not been tested extensively in the manner that EPA challenges its internal procedures before publication for regulatory applications. Candidate alternate procedures were drafted by Non-Governmental Organizations (NGOs) as generally applicable without consideration for the legal constraints placed on EPA. EPA procedures are formed around [1] legally-defined analyte lists (*e.g.*, the Priority Pollutant List), producing limited numbers of analytes, and [2] " bright-line" legal limits which define compliance vs. violation. NGOs usually do not create method criteria based on these legal constraints. This disconnect, seen between EPA and candidate alternate procedures, is to be expected. EPA has handled this problem in other media (*e.g.*, the Clean Air Act) by establishing one or more EPA reference procedures, then establishing minimum criteria for equivalency. This could be done with candidate alternate procedures if they contain statistically sound principals that allow equivalent performance.

To completely test the six criteria stated in the TSD, a tailored validation study would need to be designed and performed.

Peer Review Comments - TSD Detection and Quantification

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3. Fitzgerald, W.F.; Gill, G.A. "Sub-Nanogram Determination of Mercury by Two-Stage Gold Amalgamation and Gas Phase Detection Applied to Atmospheric Analysis," *Anal. Chem.* 1979, *15*, 1714.

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11. Eppe, G., De Pauw, E.,, *OrganohalogenCcompounds*, 2002, submitted.

12. Quantifying uncertainty in analytical chemistry, EURACHEM/CITAC Guide 2000.

13. Barwick V.J., Ellison S.L.R. "Development and Harmonisation of Measurement Uncertainty Principles. Protocol for Uncertainty Evaluation from Validation Data", VAM Project 3.2.1.

Question 7. *Has EPA dealt with the interlaboratory versus intralaboratory issues appropriately and, if not what recommendations would you make for dealing with the issues more appropriately?*

Intralaboratory Issues -

EPA has done an adequate job showing performance of EPA methods, especially defining detection (e.g, MDL). EPA has presented extensive data on interlaboratory studies that demonstrate method performance for a number of EPA regulatory procedures.

Need for a tailored demonstration study -

To fully evaluate alternate approaches a cooperative study should be performed that is designed with input from all settlement participants, and interested outside laboratory professionals. That study could include spike levels, blank and zero determination, intralaboratory variability, ruggedness testing, "pairs" determinations, use of "real world" samples, evaluation of outlier criteria, sufficient replicates to challenge statistical models, and reproducibility versus repeatability (*e.g.*, single unbroken series of determinations, versus, series performed on different dates after set up and calibration).

Since the subject legal settlement specifically addressed mercury using EPA Method 1631B, the focus of any collaborative study to answer questions raised in the TSD and legal challenges, should include this specific method. In a joint validation study, it would be useful if EPA incorporated uniform procedures to be followed for any alternate procedures that supplant EPA numbered methods.

Better method equivalency and method flexibility -

Simple equivalency procedures are routinely specified by several EPA Offices. For air determinations EPA provides a generic method protocol to demonstrate method performance. This is used to show that an alternate procedure is suitable for reporting accurate data for regulatory purposes. For stack methods, four (4) concurrent determinations in the same source are required. EPA could use this type of process to set and demonstrate simplified equivalency criteria for existing EPA water and waste water methods.

Such guidance (method equivalency and flexibility) will become more critical as detection limits are driven lower, additional analytes are required, and more complex matrices are added to areas of regulatory concern.

Interlaboratory Issues -

Need for an approved reference and audit standard -

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Interlaboratory performance is highly variable using modern ultra-trace methods like EPA Method 1631. When small batches of samples arrive at most environmental laboratories, they are scheduled in series with other methods and different analytes than mercury. These samples must be checked in, records verified, proper storage and chain-of-custody implemented. At that point the appropriate equipment must be started and calibrated. This process is the worst case, intermittent analyses where all the causes of variability, and sensitivity loss, are maximized. This means quality control on every batch of samples becomes critically important. EPA validation studies, which demonstrate the optimum method performance, are useful guidance; however, one-time optimum performance does not reflect batch-to-batch data quality in actual operation. In the real world non-optimum operation is the rule, not the exception. This problem is exacerbated with ultra-trace methods.

Better method equivalency and method flexibility -

Method 1631B is an example of a prescriptive method where form exceeds function. The criteria for any change to the method are so restrictive that no operating laboratory will make any change unless major financial support is provided to conduct the EPA required proofs. In reality,, under Method 1631B a laboratory has no option to even perform common sense changes that could lessen cost and improve efficiency. Also in Method 1631B a lone supplier is identified, and the caveat "or equivalent" is added. This causes a monopoly where cost of supplies and equipment can drive up method cost.

Example 1. Black anodized aluminum optical block -

"6.3.2.5 Black anodized aluminum optical block—holds fluorescence cell, PMT, and light source at perpendicular angles, and provides collimation of incident and fluorescent beams ***(Frontier Geosciences Inc., Seattle, WA, or equivalent).***"

Example 2. Cold vapor generator -

"6.4.4 Cold vapor generator (bubbler)—200-mL borosilicate glass (15 cm high x 5.0 cm diameter) with standard taper 24/40 neck, fitted with a sparging stopper having a coarse glass frit that extends to within 0.2 cm of the bubbler bottom ***(Frontier Geosciences, Inc. or equivalent).***"

Example 3. Gold-coated sand traps -

"6.5.2 Gold-coated sand traps—10-cm long x 6.5-mm OD x 4-mm ID quartz tubing. The tube is filled with 3.4 cm of gold-coated 45/60 mesh quartz sand ***(Frontier Geosciences Inc., Seattle, WA, or equivalent).***"

EPA could list alternate suppliers and approved alternate devices. Or even better, include specifications for alternate devices and exclude listing specific suppliers. For example gold-coated quartz wool traps have been used for mercury amalgamation for many years. Quartz wool would has much better air flow performance than sand. A gold coated quartz wool trap would have much less pressure drop than the prescribed sand trap. To use such a device would require an onerous amount of study and documentation that would deter any private laboratory.

Difficulty of making any method modifications is onerous -

Method 1631 is replete with sections that block any method changes, even the most obvious or simple. EPA Method 1631 makes modifying the method a major endeavor. This is overkill for the stated purpose, limiting changes. In reality a method which is written in this extraordinarily confining way, may spawn legal battles over minutiae in laboratory reports that show (or challenge) the smallest elements of method performance. Sections 9.1.2.2 through 9.1.2.4 speak for themselves.

Two examples from Method 1631 are given below.

Example 1.
Alternate determination methods restricted, Section 9.1.2 -

"9.1.2 If an analytical technique other than the CVAFS technique specified in this Method is used, that technique must have a specificity for mercury equal to or better than the specificity of the technique in this Method."

Example 2. Onerous requirements for even the smallest modification, Section 9.1.2.2 through 9.1.2.4-

"9.1.2.2 The laboratory is required to maintain records of modifications made to this Method. These records include the following, at a minimum:

9.1.2.2.1 The names, titles, addresses, and telephone numbers of the analyst(s) who performed the analyses and modification, and the quality control officer who witnessed and will verify the analyses and modification

9.1.2.2.2 A narrative stating the reason(s) for the modification(s)

9.1.2.2.3 Results from all quality control (QC) tests comparing the modified method to this Method, including the following:

(a) Calibration (Section 10)
(b) Initial precision and recovery (Section 9.2)
(c) Analysis of blanks (Section 9.4)
(d) Matrix spike/matrix spike duplicate analysis (Section 9.3)
(e) Ongoing precision and recovery (Section 9.5)

(f) Quality control sample (Section 9.6)
(g) Method detection limit (Section 9.2.1)

9.1.2.2.4 Data that will allow an independent reviewer to validate each determination by tracking the instrument output to the final result. These data are to include the following:

(a) Sample numbers and other identifiers
(b) Processing dates
(c) Analysis dates
(d) Analysis sequence/run chronology
(e) Sample weight or volume
(f) Copies of logbooks, chart recorder, or other raw data output
(g) Calculations linking raw data to the results reported"

In summary new EPA methods like Method 1631 may be too restrictive, especially with simple configuration issues, like specifying a specific gold sand trap by one producer, while the desorber used with that trap is very simply stated. A home-made desorber can be used and will work fine. Why not simplify other devices the same way.

"Section 6.5.3 Heating of gold-coated sand traps— To desorb Hg collected on a trap, heat for 3.0 min to 450–500 EC (a barely visible red glow when the room is darkened) with a coil consisting of 75 cm of 24-gauge Nichrome wire at a potential of 10-14 vac. Potential is applied and finely adjusted with an autotransformer."

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Question 8. *Can you recommend any improvements to the detection and quantitation procedures described in the TSD?*

The most important improvements to detection and quantification are quality control procedures that insure accurate data for specific, individual sets of samples.

Improvements will come when EPA adds defined quality control procedure to show that laboratories are actually performing these ultra trace methods at the low levels needed.

Four items will be discussed:

[1] Audit Standards,
[2] Analysis Series,
[3] MSD at two levels,
[4] Quality adherence and audit tools

1. Audit Standards

Method 1631 addressed reference materials in Section 9.6.

"Section 9.6 Quality control sample (QCS)—The laboratory must obtain a QCS from a source different from the Hg used to produce the standards used routinely in this Method (Sections 7.7–7.10). The QCS should be analyzed as an independent check of system performance."

The current Method 1631 Quality Control Sample is a calibration standard with the specific purpose of using dual calibrants from separate sources. Method 1631 also specifies calibrants traceable to NIST standards (e.g., NIST 3133, a standard mercury solution). This is adequate sourcing for calibration solutions, not for method performance.

Much more is required to show intra-laboratory method performance. An audit sample is needed of known composition and concentration. EPA should provide an audit standard along with storage guidance, stability information and validation data. This should be a standard that regulators or laboratory mangers can dilute to known concentrations for blind performance audits. This audit material should be made from multiple mercury forms to show that a performing laboratory can handle complex matrices.

The EPA Las Vegas Laboratory has been supplying audit samples, including aqueous standards, for mercury, for many years. Cinnabar is commonly found in the environment, and is considered "safe" to humans and the aquatic environment. The audit material for this program should include other mercury forms that reflect all species listed in the method (i.e., *"(Hg(II), Hg(0), strongly organo-complexed Hg(II) compounds, adsorbed particulate Hg, and several tested covalently bound organo-mercurials (e.g.,CH3HgCl, (CH3)2Hg, and C6H5HgOOCCH3)").*

2. Analytical Series

Methods like Method 1631 should define a calibration series for actual reported measurements. The EPA Contract Laboratory Program (CLP) showed the need for this approach. The CLP program used Laboratory Control Samples (LCS) to show calibration during analytical measurements. With modern instrumental autosamplers series operation is simple to perform. A series for ultra-trace mercury measurements could be the following:

> Calibration Standard (Medium Concentration), -> Calibration Standard (Low Concentration), -> Sample 1, ->Sample 2, ... -> Sample X, -> Sample Y, -> Calibration Standard (Low Concentration), -> Calibration Standard (Medium Concentration)

The initial two calibration analyses (Medium and Low Concentration Standards), would cause the analysis to be stopped if unacceptable performance is observed. The first analysis after native samples are processed, the Low Concentration Standard, is important because it shows that the analytical system did not degrade during a series of reported analyses. The higher concentration standards should not be measured first because higher analyte levels can pacify active sites and mask method failure at or near the method detection limit. Actual and measured calibration standard values should be reported.

This LCS series should be reported as a measurable quality performance criterion.

3. Matrix Spike Duplicate (MSD)

Other regulatory bodies have abandoned the MSD criteria. A duplicate analysis (one degree of freedom) provides little or no useful information. This is a time-wasting, cost escalating step in many EPA numbered methods.

Some European authorities have dropped the traditional EPA method spike duplicate (MSD). They specify two different spike levels instead, one near the MDL and a second spiked matrix sample above the MDL, at a concentration of linear response. Method 1631 extensively defines low and intermediate spiking levels, so this approach could easily be used with Method 1631.

A stronger quality control approach would be to analyze a reference sample (previously discussed) from a recognized metrology authority (*e.g.*, NIST, BCR), or through the EPA contract program for reference standards, along with a matrix spike near the MDL. This

would be performed with every batch of 20 samples or once during the month in which less than 20 samples are analyzed. Thereby three quality control objectives could be included: matrix effects, low level detection in the matrix tested, and performance with a reference material.

At a minimum matrix spike analyses should be performed on each group of samples that represent either a different matrix, or a separate sample batch. From a regulatory perspective it would be useful if EPA defined what constitutes a discrete matrix, including that definition in the method itself. This would prevent a large batch of samples from different sources being analyzed together and only one matrix tested.

4. Quality adherence and audit tools

Since staff training and experience vary, and Methods like 1631 are performed at irregular intervals, audit and adherence tools would help EPA gain consistency in method performance. Three tools are suggested:

[1] Flow Charts,
[2] Audit Checklists,
[3] Control Charts.

1. Flow Charts

Modern methods like Method 1631 are very complex due to the very low measurement levels attained. Prescriptive steps for Method 1631 include:

Method detection limit demonstration	(Section 9.2.1),
Initial precision and recovery (IPR)	(Section 9.2.2),
Matrix spike (MS) and matrix spike duplicate (MSD)	(Section 9.3),
Ongoing precision and recovery (OPR)	(Section 9.5.

A set of simple flow charts could be developed to visually show the order of method steps. This would be a valuable training aide, which would also help analysts set up and perform Method 1631 on irregular schedules.

2. Audit Checklists

Audit checklists are valuable tools for everyone performing these complex methods or verifying laboratory performance. EPA could develop audit checklists (*e.g.*, necessary procedures, quality control data, *etc.*) as part of the method development process. This would provide a uniform document for checking method adherence.

3.Control Charts

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Control charts are useful for environmental laboratories routinely conducting trace analytical procedures. EPA could establish criteria for control charts. This would allow laboratories to flag method failure by measuring intra-laboratory error bands for acceptable performance over time. EPA has extensive experience with control charts, and this would be a simple addition to Method 1631.

Summary Statement

EPA has done an exemplary job of communication with the regulated community through "out reach" programs associated with Method 1631. Several supporting documents like Guidance for Implementation and Use of EPA Method 1631 for the Determination of Low-Level Mercury (40 CFR part 136) (EPA 821-R-01-023, March 2001), and Method 1669 ("Sampling Amb ient Water for Trace Metals at EPA Water Quality Criteria Levels") are examples of valuable supporting tools EPA provides.

Through public meetings, training, and documents, EPA staff help practitioners master the challenges of sampling, clean containers, field and laboratory blanks, handling ultra trace metals samples, and conducting these difficult tests. EPA is commended on the way they have publicly communicated technical issues associated with complex new methods like Method 1631.

APPENDIX H

Walter W. Piegorsch
Comments

28 August 2002

Peer Review Report on: U.S. EPA Technical Support Document of Detection and Quantitation Regulations under the Clean Water Act

The Technical Support Document (TSD) is well-organized and intelligently thought-out. It has strong scientific merit and establishes a good baseline from which further discussion and debate may continue on the important issue of detection limits and quantification of contaminants in the nation's water supply. I do have selected concerns with portions of the narrative, however, and these are listed within my specific responses, below. (Item numbers correspond to questions raised in the Charge to Peer Reviewers.)

1. EPA's willingness to consider other detection and quantification concepts is admirable. On balance, I am comfortable with the broad-based concepts already discussed in the TSD, although I do have some concerns with specific implementation. These are detailed in item #2, below.

2. In Ch. 3 of the TSD, many important issues are listed for evaluating detection and quantification limit concepts. I applaud the EPA's desire to consider alternative (quantitative) perspectives. In this vein, and accepting the TSD's interpretation of the MDL as a "general purpose version of Currie's critical values [L_C]" (p.2-3), I am concerned that the operational definition as taken from pp. 5-2/5-3 of MDL = $t_{0.99}(\mathrm{df})S$, where df is an appropriately-chosen value for the degrees of freedom and S is an associated root mean square, does not correspond to an appropriate form of interval estimator. (Note, by the way, that the definition of S^2 given on p.5-2 is in error. The correct expression should be

$$S^2 = \frac{1}{n-1}\left[\sum_{i=1}^{n} X_i^2 - \frac{\left(\sum_{i=1}^{n} X_i\right)^2}{n}\right].$$

I assume that this a typographical error and not a more serious misinterpretation of statistical principles.) Indeed, I am forced to argue against the comments at the top of p.5-3 that a "95% confidence interval for the ... MDL..." can be calculated, since I cannot interpret or determine what such an inference would provide. Technically, a confidence interval is a set of values of some (unknown) parameter that satisfies a $1-\alpha$ coverage probability restriction. I do not know what "parameter" a "95% confidence interval for the ... MDL" is covering, since the MDL is apparently itself defined as a form of upper interval limit. (The comment on p.5-4 that "...confidence intervals about the estimated MDL ... are expression of uncertainty in the estimates" hints at what may be meant here: that some recognition is needed that the MDL is a statistical quantity subject to random variation, and not a true, known, fixed value. But, the idea of building a confidence interval "about" it is fallacious; much more careful reasoning and explanation is needed here.

As far as I can tell, the broader literature on MDL estimation suggests that what is desired when calculating an L_C value (such as the MDL) is some form of (upper) prediction or tolerance limit. Some authors even argue that the Glazer *et al.* model and definition of the MDL does not even produce a valid confidence, prediction, or tolerance interval. Rather than join the fray here,

however, I suggest the following reconsideration: Accepting the TSD's argument on p.3-25 that the practical value of tolerance limits for this sort of analyte detection is limited, one naturally thinks to view the MDL as a prediction limit. But, as Gibbons (1994, p.98) points out, a single-use prediction limit of such a form should contain an additional term, viz.

$$t_{0.99}(\mathrm{df})S\sqrt{1 + \tfrac{1}{n}} \ .$$

I emphatically encourage the EPA to revisit its definition of MDL with this consideration in mind.

Based on my own experience, I think the single most problematic issue is that of correction for false negatives when developing a detection limit. For the generic problem of detecting a chemical analyte, the incorporation of false negatives should be afforded greater importance than I think the TSD provides. As the TSD appears to recognize, the work of Clayton *et al.* (1987) appears to be a primary source for proper conversion of a L_C value into a L_D value. Having said this, I will say that for the specific problem of detecting mercury contamination and how it affects water quality, and for that matter, of detecting hazardous agents in the country's water supply, one might view the TSD's emphasis on L_C-type values such as the MDL (if correctly calculated) as a form of implicit conservatism ('erring on the side of caution,' if you will). Viewed from this perspective, the discussion of false negatives and the motivation behind the EPA's current strategy as put forth in §3.3.6 is persuasive. Nonetheless, I would encourage the TSD to reconsider and revisit the importance of false-negative correction and use of a L_D values in practice.

In passing, note also that *if* the use of tolerance limits is in fact desired, then Gibbons' (1994, p.99) presentation would be appropriate for consideration.

There is also the rather strong argument that instead of L_C calculation from a single concentration design, use of calibration designs is felt to be more efficient in terms of deriving effective detection limits from the data (Clayton *et al.*, 1987; Gibbons, 1994, §5.3). Although I am cognizant of the claim that such designs greatly increase the cost and resource requirements for monitoring and detecting contaminants in the water supply, I also think that if any area required maximal assurance of drinking water quality, detection of mercury contamination would sit high on the public's list. Perhaps the agency should to revisit this issue within the context of this perspective.

3. The evaluation criteria in Ch. 4 do seem reasonable at first reading. I do not think any of them should be eliminated, and I do not have any concrete suggestions for addition. In passing, however, I should note that as I continued through the chapter, I found it perchance-less-than-coincidental that the (revised) MDL and ML concepts seemed to satisfy the criteria so readily, and that most of the other concepts were found wanting. (A cynical reader might view this as a contrivance that elevates the MDL and ML at the expense of the other methods, and perhaps the EPA may wish to proceed with caution in this area.)

4. The assessment of the various detection and quantification concepts in Ch. 5 is reasonable, given the use of the criteria as presented in Ch. 4. However, added consideration of the comments in item #2, above, would cause an important reconsideration in the assessment.

5. I am hesitant to admit formal acceptance of the conclusions presented in Ch. 6 until the issues raised in item #2, above, are brought into further consideration.

6. I would encourage the EPA to expand its search and consider as many additional data sets as can be acquired in a reasonable period of time. Unfortunately, however, I am unable to recommend any such.

7. The issues of intralaboratory and interlaboratory variation are quite important, and I applaud the TSD for its consideration of them. While reasonably addressed, I would encourage that the EPA undertake, commission, or actively abet a formal interlaboratory study, building on the success of the Method 1638 Interlaboratory Validation Study. The recognition that multiple component of variation can exists in calculating L_C (or any other form of detection/decision limit), is an important one, and such calculations must be based on appropriate variance components for the model under study (Gibbons, 1995). A large, carefully-conducted interlaboratory study would make a major contribution towards understanding and quantifying these components for use in future detection limit calculations.

8. Aside from the comments given above, I have no further improvements to suggest. I do have one general question, however: has the EPA studied the use of composite sampling methodology (primarily from a statistical perspective) for application to MDL or ML determination? I do not profess to be an expert in composite sampling, and perhaps I missed this in the TSD, but as I understand it composite sampling is intended for chemometric and environmental monitoring scenarios where chemical analytes or biochemical (and also pharmaceutical) metabolites are assessed for levels of occurrence. Apparently, it is particularly useful when studying whether a chemical has exceeded or dropped below some critical threshold. Other uses include compliance monitoring for environmental standards (Barnett and Bown, 2002), classification of samples as to their levels/status of some environmental contaminant (Johnson and Patil, 2001). This background seems similar tot he detection limit problem under considered here, and this methodology may prove useful.

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Gibbons, R. D. (1994). *Statistical Methods for Groundwater Monitoring.* New York: John Wiley & Sons.

Gibbons, R. D. (1995). Some statistical and conceptual issues in the detection of low-level environmental pollutants (with discussion). *Environmental and Ecological Statistics* **2**, 125-167.

Johnson, G. D., and Patil, G. P. (2001). Costs analysis of composite sampling for classification. *Environmental and Ecological Statistics* **8**, 91-107.

16 September 2002

It is unfortunate that the Agency was uncomfortable with my previous report. In keeping with their specific request, I have returned to the eight Questions to Peer Reviewers and have attempted to reemphasize my replies in a targeted, direct, and unambiguous manner. These follow:

1. I remain comfortable with the broad-based concepts discussed in the TSD. As mentioned previously (in my earlier reply to Question 8), however, the EPA should build into its mercury detection strategy — and elsewhere as they see fit — a review and critique of how the use of composite sampling would improve MDL and/or ML determination(s). Besides the references in my previous comments, additional sources of input on this topic include the following:

Boswell, M. T., Burnham, K. P., and Patil, G. P. (1988). Role and use of composite sampling and capture-recapture sampling in ecological studies. In *Handbook of Statistics Volume 6: Sampling*, Krishnaiah, P. R. and Rao, C. R. (eds.), 469-488. Amsterdam: North-Holland/Elsevier.

Boswell, M. T., Gore, S. D., Lovison, G., and Patil, G. P. (1996). Annotated bibliography of composite sampling Part A: 1936-92. *Environmental and Ecological Statistics* **3**, 1-50.

Correll, R. L. (2001). The use of composite sampling in contaminated sites—a case study. *Environmental and Ecological Statistics* **8**, 185-200.

Dorfman, R. (1943). The detection of defective members of large populations. *Annals of Mathematical Statistics* **14**, 436-440.

Edland, S. D., and van Belle, G. (1994). Decreased sampling costs and improved accuracy with composite sampling. In *Environmental Statistics, Assessment, and Forecasting*, Cothern, C. R. and Ross, N. P. (eds.), 29-55. Boca Raton, FL: Lewis Publishers.

Elder, R. S., Thompson, W. O., and Myers, R. H. (1980). Properties of composite sampling procedures. *Technometrics* **22**, 179-186.

Gore, S. D., Patil, G. P., Sinha, A. K., and Taillie, C. (1993). Certain multivariate considerations in ranked set sampling and composite sampling designs. In *Multivariate Environmental Statistics*, Patil, G. P. and Rao, C. R. (eds.), 121-148. Amsterdam: North-Holland.

Kosmelj, K., Cedilnik, A., and Kalan, P. (2001). Comparison of a two stage sampling design and its composite sample alternative: An application to soil studies. *Environmental and Ecological Statistics* **8**, 109-119.

Kotz, S., Johnson, N. L., and Read, C. B. (1982). Bulk sampling. In *Encyclopedia of Statistical Sciences, 1*, Kotz, S., Johnson, N. L. and Read, C. B. (eds.), 324-325. New York: John Wiley & Sons.

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Nussbaum, B. D., and Gilbert, R. O. (2001). Editorial: Special issue on composite sampling. *Environmental and Ecological Statistics* **8**, 89-90.

Patil, G. P., Gore, S. D., and Sinha, A. K. (1994). Environmental chemistry, statistical modeling, and observational economy. In *Environmental Statistics, Assessment, and Forecasting*, Cothern, C. R. and Ross, N. P. (eds.), 57-97. Boca Raton, FL: Lewis Publishers.

2. Reemphasizing my previous comment: the operational definition as taken from pp. 5-2/5-3 of MDL = $t_{0.99}(\mathrm{df})S$ does not correspond to a confidence statement that I can interpret. (See Question #4, below.) This should be replaced, although I agree that a number of statistical quantities could be used; this is where the "fray" seems to be most boisterous. (By the way, the

TSD, and I, should be more careful in the use of statistical terminology. We both refer often to confidence "intervals," when in fact the quantity of interest is a confidence limit — or tolerance limit, etc. — on some underlying parametric quantity.) I see no reason to change the core of my previous recommendations, however. If we accept the TSD's argument on p. 3-25 that the practical value of tolerance limits is limited, then the MDL should be viewed as a prediction limit. And if so, it must contain an additional term as per Gibbons (1994, p. 98):

$$t_{0.99}(\mathrm{df})S\sqrt{1 + \frac{1}{n}} \; . \qquad (1)$$

Also, to reemphasize, the single most problematic issue when developing a detection limit is correction for false negatives. I took from the TSD (in §3.3.6) an implicit emphasis on L_C-type values such as the MDL [when correctly calculated, as in (1)], as motivated by an underlying sort of practical/environmental conservatism that essentially removes false negatives from the estimator's development. I am willing to accept this interpretation. I suspect the fray will continue, however, since there seems to be a fair amount of confusion on the issue in the analytical chemistry literature. The bottom line from my reading of the TSD is that, in effect, we are calculating an L_C, but using terminology that makes some readers think it's an L_D. I can accept the argument that false negative errors are not the critical issue here, and hence that the approach is reasonable (once correct calculations are undertaken). But, the Agency should put forth an effort to overcome this confusion in terminology. (I expect they will ask me how, and in reply I'd suggest emphasizing that an L_C calculation is a form of decision limit, not a detection limit. But here I suspect many users will still confuse the terms, or reverse their meaning, or not see the difference, or who knows what else? I don't know how winnable this battle is...)

One caveat: although I think the prediction limit argument is acceptable, *if* the use of tolerance limits rather than prediction limits is in fact desired, then Gibbons' (1994, p. 99) presentation or an equivalent approach should be used instead to correct the MDL calculation.

Also, as requested, here are some other sources from the literature (besides those already listed on TSD pp. R-1/R-2) that have commented in various ways on the issue of detection/decision limits in environmental applications. The van der Voet (2002) entry expands upon this list somewhat. I'm sure some of them will already be familiar to the Agency.

Adams, M. J. (1992). Errors and detection limits. In *Methods of Environmental Data Analysis*, Hewitt, C. N. (ed.), 181-212. Amsterdam: Elsevier Applied Science.

Clark, M. J. R., and Whitfield, P. H. (1994). Conflicting perspectives about detection limits and about the censoring of environmental data. *Water Resources Bulletin* **30**, 1063-1079.

Cressie, N. (1994). Spatial chemostatistics. In *Environmental Statistics, Assessment, and Forecasting*, Cothern, C. R. and Ross, N. P. (eds.), 131-146. Boca Raton, FL: Lewis Publishers.

Currie, L. A. (1988). *Detection in Analytical Chemistry: Importance, Theory, and Practice*. New York: American Chemical Society.

Currie, L. A. (1996). Foundations and future of detection and quantification limits. *Proceedings of the American Statistical Association, Section on Statistics and the Environment*, 1-8.

El-Shaarawi, A. H., and Naderi, A. (1991). Statistical inference from multiply censored environmental data. *Environmental Monitoring and Assessment* **17**, 339-347.

Gibbons, R. D. (1994). *Statistical Methods for Groundwater Monitoring*. New York: John Wiley & Sons.

Gibbons, R. D. (1995). Some statistical and conceptual issues in the detection of low-level environmental pollutants (with discussion). *Environmental and Ecological Statistics* **2**, 125-167.

Helsel, D. R. (1990). Less than obvious: Statistical treatment of data below the detection limit. *Environmental Science & Technology* **24**, 1766-1774.

Lambert, D., Peterson, B., and Terpenning, I. (1991). Nondetects, detection limits, and the probability of detection. *Journal of the American Statistical Association* **86**, 266-277.

Maynard, A. W. (1990). Environmental tests: Are they valid? *Chemical Technology* **20**, 151-155.

McBean, E. A., and Rovers, F. A. (1998). *Statistical Procedures for Analysis of Environmental Monitoring Data & Risk Assessment*. Upper Saddle River, NJ: Prentice Hall PTR.

Millard, S. P., and Neerchal, N. K. (2001). *Environmental Statistics with S-PLUS*. Boca Raton, FL: Chapman & Hall/CRC.

Nagaraj, N. K., and Brunenmeister, S. L. (1994). A new approach for accommodation of below detection limit data in trend analysis of water quality. In *Environmental Statistics, Assessment, and Forecasting*, Cothern, C. R. and Ross, N. P. (eds.), 113-127. Boca Raton, FL: Lewis Publishers.

Slyman, D. J., de Peyster, A., and Donohoe, R. R. (1994). Hypothesis testing with values below detection limit in environmental studies. *Environmental Science & Technology* **28**, 898-902.

van der Voet, H. (2002). Detection limits. In *Encyclopedia of Environmetrics, 1*, El-Shaarawi, A. H. and Piegorsch, W. W. (eds.), 504-515. Chichester: John Wiley & Sons.

3. The evaluation criteria in Ch. 4 seem reasonable. I would not delete any of them.

4. The assessment in Ch. 5 should be revisited with the goal of including the issues I note in Question #2 above. In particular, if equation (1) or some other new limit calculation is adopted then clearly it too should be placed under a similar evaluation.

As for specific positive and negative features:

• As I mentioned previously, that the definition of S^2 given on p. 5-2 is in error. A correct expression is

$$S^2 = \frac{1}{n-1}\left[\sum_{i=1}^{n} X_i^2 - \frac{\left(\sum_{i=1}^{n} X_i\right)^2}{n}\right].$$

• As noted above, on p. 5-3 (lines 2 and 13) the suggestion that MDL represents a 95% confidence interval is spurious. I do not see how in its given form it corresponds to an appropriate form of interval estimator (and, as also mentioned above, it's a limit, not an interval). Technically, a confidence statement provides a limit or interval on some parameter, say θ, or parametrically-related quantity. I do not see which such quantity $t_{0.99}(df)S$ or $2.681S_{pooled}$ is intended to bound. This issue also pertains to the discussion on Condition 3 on p. 5-4. (Although, the issue raised there about "uncertainty in the estimates" is a valid argument.) These concerns lead me to suggest the revision to the prediction limit construction in equation (1).

• On the positive side, it is good to mention (p. 5-4, middle) that the MDL procedure is not adjusted for outliers, since this sort of subtlety could escape the casual reader.

• (p. 5-8, top) I agree that the IDE procedure as outlined is so complex as to make simple determination of error rates associated with it untenable. This point is worth emphasizing.

• I liked the description of the IUPAC/ISO detection limit (starting on p. 5-14). Similarly, I thought the introduction to quantitative assessment of the ML (p. 5-17) was concisely presented.

5. As previously, I cannot formally accept the conclusions presented in Ch. 6 until the issues raised in Question #2, above, are addressed.

6. Since I do not have at my disposal any new data sets, nor am I working with anyone currently who does, I cannot give the EPA any new sources of data. However, as suggested previously, the more data sets the Agency can put forth as having been studied, the stronger the overall effort will appear.

7. The recognition that multiple component of variation can exist in calculating L_C (or any other form of detection/decision limit) is an important one. As suggested previously, I think the EPA should undertake, commission, or actively abet a formal interlaboratory study, building on the success of the Method 1638 Interlaboratory Validation Study. A large, carefully-conducted interlaboratory study would make a major contribution towards understanding and quantifying these components for use in future detection limit constructions.

8. I have no further comments.

APPENDIX I

Dr. David M. Rocke
Comments

Review and Comments on *Technical Support Document for the Assessment of Detection and Quantitation Concepts*

David M. Rocke

Questions Posed

1. The list of detection and quantitation concepts is sufficiently complete for this analysis.

2. The issues are complete as laid out in Chapter 3.

3. The evaluation criteria in Chapter 4 are adequate. However, I believe some changes should be made to criteria 4 and 5 as outlined below in the comment section. Criterion 4 should be edited to reflect its essential equivalence to an implementation of Currie's critical level. Criterion 5 should be completely changed to reflect the fact that almost all implementation of limits of quantitation have nothing to do with whether the measurements are actually quantitative.

4. The method assessments in Chapter 5 are sound (subject to comments below on particulars of the MDL).

5. The conclusions in Chapter 5 are generally reasonable. With a slight alteration to the specifications on the spike concentration (see below), the EPA MDL as now given is a reasonable, practical implementation of a limit of detection concept and method. None of the other methods is an improvement on this overall. With respect to the limit of quantitation concept, the EPA ML is as good as any of the others given; however, all are flawed by the assumption that there is some level higher than the critical level needed before quantitative assessments can be made. This is not supported in this document, nor anywhere else I have seen, except as an almost unexamined assumption. The entire concept of a quantitation level higher than the critical level should be immediately discarded.

6. There is no need to examine additional data sets.

7. The EPA's position on interlaboratory vs. interlaboratory variability is reasonable. See comments below.

8. See comments below on the MDL.

Comments

1.3.2

Grouped analysis by concentration leads to anomalous results. If all the samples at a given concentration are analyzed in sequence, then the next concentration, and so on, the values at a given concentration will be closer together than would be the case if they were analyzed at different times, or interspersed with other concentrations. We have seen this phenomenon many times in such data. This means that the variability of the replicates around the mean of the replicates is an underestimate of the actual variability at that concentration. This problem should be fixed by using a proper randomized-order design, but can be mitigated by always looking at variability around the calibration line, rather than around the mean of the replicates (cf. 3.3.8.2).

2.2.1

The MDL had a number of problems that needed repair, some of which were fixed in the rewording on page 5-4. The basic concept of Glaser et al. (1981) that the "MDL is considered operationally meaningful only when the method is truly in detection mode, i.e., [the] analyte must be present." is problematic. For methods under which a signal is generated from blanks, this is not at all necessary. For cases in which the blank does not generate a signal due to instrumental limitations (such as inability to find the peak to integrate), one must generate the MDL using positive concentrations. Otherwise, blank samples are fine. See further comments below on the MDL.

2.2.2

The ML as originally defined may very well be below the MDL. After all, the concentration at which the MDL is measured must generate peaks that can be measured. Any definition that relates the ML or related concept to either a multiple of the standard deviation at zero, or to a desired CV is fundamentally flawed. If the instrument can be read, and the spectra can be recognized, then the ML is exceeded, regardless of the other issues. I don't think it is too much to say that any level at which the instrument can be read, and at which there is a reliably estimated standard deviation is a level at which quantitation is possible. No arbitrary standard regarding multiples of the standard deviation at zero or a desired CV is appropriate for any purpose in analytical chemistry or the regulation of toxic substances. This includes the PQL, the AML and other related methods. None of them generate a useful number.

Regulatory Levels

Obviously, levels of a toxic substance can not easily be regulated below the level at which there is instrumental response (i.e., a signal is generated). All environmental measurements should be reported as measured, and should only be reported as non-detects if the instrumental response itself fails. If a value is generated by the instrument, it should be reported, with an indication of what the estimated standard deviation is, and

whether the measurement shows the concentration to be non-zero (that is, whether the signal is above the critical level). See 3.3.2. For substances in which the toxic level is well below the critical level, then the compliance threshold should be at the critical level (in one of its implementations such as the revised MDL).

Interlaboratory Variability

If a laboratory computes its critical level using a procedure such as the MDL, it makes no sense to expand this to account for interlaboratory variability. Whether other labs can or cannot detect the substance with a signal at the MDL of the given laboratory is irrelevant. It may be different if the goal is precisely to determine the quantity of the analyte in a standard sample. In this case, interlaboratory variability may be appropriately considered. It should not be considered in detection decisions unless it can be shown that such decisions in an individual laboratory are biased and may over- or under-estimate the true critical level (detection threshold) in that laboratory. For the specific purpose of determining whether a given sample exceeds the safe level, a general interlaboratory study is not of much use, since it may be influenced by the performance of laboratories at levels far removed from the point at issue. If the safe level is below the critical level, than use of the critical level is appropriate as an action threshold. If the safe level is above the critical level, then interlaboratory variation should only be taken into account if it can be shown that the number of false positives when the analyte is present at the safe level is not well controlled using the usual intralaboratory calibration methods.

Prediction and Tolerance Intervals

Tolerance intervals are inappropriate for environmental monitoring. The main issues here are 1) is the true concentration greater than some specified safe of action level, with sufficient confidence, and 2) what interval of possible concentrations is consistent with one or a series of measurements, with a specified degree of confidence. Both are statements about a given sample or series of samples, and not about the hypothetical variability of future estimates. Suppose that one has a sample of 10 observations with mean concentration of 1ppb and standard deviation of 0.5ppb. Then the estimated 99% critical level is (2.326)(0.5) = 1.2ppb. One may choose to use a t-score instead of a normal score so that the chance that a future observation will exceed this level is in fact 99%. In this case, the critical level estimate would be (3.250)(0.5) = 1.6ppb. This does actually correspond to a prediction interval for future observations from a zero concentration sample.

If one asked instead for a 95% confidence interval for the .99 percentage point of the true distribution of measurements (assuming normality) when the true quantity is zero, this can be calculated approximately using a chi-squared distribution and covers the interval (0.9ppb, 2.4ppb). It does not, however, make sense to use 2.4ppb as a threshold, since the chance of a future observation exceeding 2.4ppb when the true mean concentration is 0 is about .0005, far smaller than the intended false-positive limit of .01.

4.4 Criterion 4

This criterion appears from the description and the discussion to be a mix of the Currie concepts of critical level and minimum detectable value. What should appear here is the critical-level equivalent. Here is a suggested re-wording:

The detection level concept should identify the signal or estimated concentration at which there is 99% confidence that the substance is actually present when the analytical method is performed by experienced staff in a well-operated laboratory.

4.5 Criterion 5

This concept has no operational meaning as written. The only real criterion for a QL is that the instrument should generate a recognizable signal. Here is a suggested re-wording:

The quantitation limit concept should identify a concentration at which the instrument yields a measurable signal at least 99% of the time, and which is also no smaller than the detection level. This will often be the same as the detection level.

Evaluation of Detection Limit Concepts: The MDL

This method, as re-described in Condition 3 on the top of page 5-4, and as further specified on page 5-2, is a reasonable implementation of the critical level concept for situations in which the instrument may not yield reliable data for blanks. It should not increase the critical level much over what would be obtained using true blanks if that were possible. However, the use of as much as five times the critical level for the spike concentrations could be problematic. The inflation of the MDL by using a spike at the critical level is only 25% for a method with a high-level CV of 20% (this and other calculations here are done with the Rocke and Lorenzato 1995 variance function assuming a sample size of 7). A spike concentration of 3 times the critical level inflates the MDL to a value 140% higher, which even there may be tolerable. Use of a value 5 times the critical level gives an inflation of over 280%. Thus if the true critical level is 1ppb, then the use of 1, 3, and 5 times the critical level for spike concentrations in determining the MDL gives likely values of 1.2ppb, 2.4ppb, and 3.8ppb, respectively. These number were determined as follows: Let $V(y) = a^2+b^2\mu^2$. Then the expected MDL if blanks were used is approximately ta, where t is the appropriate t-statistic. If spikes at kta are used, then the variance at that level of μ is $a^2+(ktab)^2$, and the approximate estimated MDL will be t times the square root of this quantity, so that the ratio of the MDL with blanks to the MDL at spike level $\mu = kta$ is $\sqrt{[1+(ktb)^2]}$. Thus, I would recommend that the procedure be altered to use concentrations that are no more than 3 times the detection limit, and perhaps to permit concentrations lower then the critical level, including possibly blanks.

Other than that, the MDL procedure, with its new definition, is quite a reasonable choice for a detection limit concept.

APPENDIX J

Dr. A. Dallas Wait
Comments

September 19, 2002

Mr. Mike Nelson
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RE: Peer Review of the Technical Support Document for the Assessment of Detection and Quantitation Concepts

Dear Mike:

Enclosed are my peer review comments pertaining to an EPA draft document you provided me entitled " Technical Support Document for the Assessment of Detection and Quantitation Concepts." As you are aware, my opinions are based on my experience as a former practicing environmental analytical chemist, and more recently as a consultant dealing, in part, with issues regarding method design and evaluation, as well as data usability and integrity. As a senior chemist and Vice President of a nationally recognized environmental contract laboratory during the late 1970s and 1980s, I was directly involved with many of EPA's offices, including the Effluent Guidelines Division, during the formative years of regulatory method development. Since 1989 I have mostly worked with industry and attorneys, often in the context of litigation, on matters involving the integrity and admissibility of environmental data. As such, I believe my opinions are balanced between the need to use sound science, the needs of a laboratory to use defensible, yet efficient analytical methods, the needs of regulatory agencies to develop standards that ensure the safety of the public, and the needs of industry for fair and reasonable standards.

1. General comments and overall impression of the scientific merit of the document.

The crux of the Alliance of Automobile Manufacturers, Inc. et al. *v.* Carol Browner settlement agreement involves the age-old battle between theoretical science and practical science, with both sides waving the flag of sound science. The Legislative Branch has recently joined the fray by acknowledging the importance of data quality in an amendment attached to a law enacted by the 106th Congress [PL106-554]. The law, known as the "Data Quality Act" or the "Information Quality Law," mandates that the Office of Management and Budget (OMB) issue guidance to Federal agencies for "ensuring and maximizing the quality, objectivity, utility, and integrity of information (including statistical information) disseminated by federal agencies." In turn, OMB has mandated Federal Agencies such as EPA to implement data quality guidelines by October 1, 2002. I believe the construct of EPA's Technical Support Document (TSD) is consistent with the spirit of this law, as it should be. In addition, EPA should be applauded for invoking the Daubert factors (testing and validation, peer review, rate of error, and general acceptance in the scientific community); a ruling about which I have previously written opinions (See, Brilis, Worthington and Wait, "Quality Science in the Court Room: US EPA Data Quality and Peer Review Policies and Procedures Compared to the Daubert Factors [Environ. Forensics 1:197-203], and Wait, "Environmental Forensic Chemistry and Sound Science in the Courtroom [Fordham Environ. Law Journal 12:293-327]). The use of the Daubert approach is defensible and should give the resultant consensus document long-term standing.

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Overall, I believe the TSD effort is a rigorous, open and honest attempt by EPA to resolve a technically and operationally difficult matter in a manner fair to all sides.

2. Responses to specific questions outlined in the technical charge

i. In Chapter 2, EPA recognizes and is willing to accept other detection and quantitation concepts, and has attempted to identify concepts that have been widely used or are widely known. Are there other concepts and procedures that EPA should evaluate?

EPA's discussion about the historical development of detection limit and quantitation concepts is consistent with my recollection of events over the past three decades. The thoroughness of the on-line search for relevant documents provided in the Reference Section and Appendix A of the TSD was impressive. A review of my files on MDLs found nearly every paper to be listed in Appendix A. However, on-line searches often don't capture information contained in text and reference books (e.g., Budde's 2001 book entitled "Analytical Mass Spectrometry"). Has this area of information been adequately addressed by EPA?

EPA appears to have closely examined the detection and quantitation approaches by other professional organizations. Has EPA rigorously examined how these concepts are perceived and implemented by other federal and state agencies (e.g., USGS, NRC, FDA, DOD, DOE)? For example, Chapter 19 of the recently published draft document entitled "Multi-Agency Radiological Laboratory Analytical Protocols Manual" (MARLAP) discusses detection and quantitation issues. It would be useful for EPA to tabulate the concepts used by federal and state agencies in this Section of the TSD.

Another source of information may be Case Law. Has EPA examined whether there is a legal record detailing EPA (and others, e.g., NEIC, DOJ) opinions on these matters? If so, their opinions and those of the Court should be acknowledged.

Technically, EPA should justify why 7 replicates were chosen to determine MDLs rather than 6, 8 or some other number (refer to Section 2.2.1). For example, although Canada has closely mimicked EPA's MDL approach, they use 8 replicates rather than 7 ("Ontario Ministry of Environment Estimation of Analytical Method Detection Limits (MDL) – Analytical Method Detection Limits Protocol for Municipal and Industrial Strategy for Abatement (MISA) Program" [ISBN 0-7729-4117-3]).

ii. In Chapter 3, has EPA adequately identified and characterized the issues that need to be considered when evaluating detection and quantitation limit concepts in the context of implementation under the Clean Water Act? Are there any issues discussed that are not critical and can be deleted?

Matrix effects are an extremely critical element to be considered when generating MDLs. As EPA notes, since each environmental sample is unique, it would be impossible to conduct a MDL study on each. The best means of dealing with this reality is by employing on a project by project basis a graded approach to verifying MDLs. The EPA DQO process is an efficient mechanism for addressing the variability of MDLs between different matrices. As a corollary, "EPA believes that reference matrices should be used to establish method detection and quantitation

limits ..."(pg 3-4). Has EPA considered establishing a repository of "typical" matrices where low background concentrations of contaminants are thoroughly characterized similar to NIST SRMs? If laboratories had the option of evaluating MDLs using matrices similar to samples they were studying (e.g., POTW wastewater, salt water, river sediment, pond sediment, clay), this would give labs an option in demonstrating their analytical capabilities in a fashion comparable to other labs. Their use would not preclude the basic need for determining MDLs using reagent water, nor matrix specific MDLs. Again, the use of these low level matrices would be determined during the DQO process.

Section 3.2.4 discusses, in part, the option of using performance standards over prescriptive standards, which would allow laboratories and others the freedom to use a variety of different approaches to establish limits. Although theoretically this sounds agreeable, operationally this would be a nightmare and comparability, a QA tenet, would be jeopardized. I'm not in favor of this approach.

Overall, the analytical chemistry, CWA regulatory issues, and statistical issues presented in this Section of the TSD are comprehensive. The issues of integrated error are recently becoming more appreciated by analytical chemists. In Section 3.3.1, the discussion on sources of variability could be enhanced to address the impact of variability at the MDL and how this variability impacts data use. Refer to the error concepts recently discussed by EPA's Deanna Crumbling and a soon to be released paper by Dr. John Maney in the October 1 issue of Environ. Sci. & Tech.

Although informative, Section 3.1.4, which discusses measurement quality over the life of a method, could probably be deleted without hurting the integrity of the Chapter.

iii. **Do the evaluation criteria in Chapter 4 adequately reflect the discussion of issues identified in Chapter 3? Do you believe EPA should eliminate any of the six evaluation criteria or add other criteria?**

All of the criteria used by EPA are pertinent to the evaluation of viable detection and quantitation limit methods. Again, the recognition of the role of the Daubert approach (Criterion 1) is particularly important. Criterion 3 is obvious and necessary (practical and affordable procedure that a single lab can perform). The recent problems with lab fraud, as enunciated by EPA's Inspector General, Nikki Tinsley, in an open letter to the laboratory community (September 5, 2001; www.epa.gov/oigearth/eroom.htm) make the use of practical and efficient methods of key importance.

The explanations for each criterion are reasoned and persuasive. I would not remove any criteria from the evaluation process. No other evaluation criteria are apparent.

iv. **Is the assessment in Chapter 5 of the TSD valid? Are the detection/quantitation concepts presented in the chapter conceptually and operationally sound? Identify positive and negative features and justification of your conclusions.**

The thorough evaluation process used by EPA is excellent! A comprehensive and open discussion was performed for all 5 detection limit concepts and 4 quantitation limit concepts. These discussions fairly debate the pros and cons of each concept.

In Section 5.1.1.2.1, EPA astutely notes that many people complain that MDLs can vary depending on spike levels used, based on the mistaken assumption that spike levels may be arbitrarily selected. I have witnessed this same complaint numerous times. EPA also properly notes that Step 1 of the MDL procedure specifies a number of criteria that must be met in selecting spike levels. Apparently many chemists just don't get it. It would be advantageous for EPA to embellish Step 1, possibly with examples, to make the requirement clearer.

v. **Do you agree with the conclusions presented in Chapter 6?**

The discussions and findings provided in Chapter 6 are consistent with the approach, analysis and results presented throughout the TSD. Most of the assessments provided by EPA are reasonable and defensible. With regards to alternative MDL and ML procedures for stakeholders operating under CWA programs, what options is EPA considering and how does this stand up from a comparability standpoint between stakeholders? Can you give an example? I realize that there is a discussion of this issue in Section 4.6 of the TSD, but I'm having a difficult time understanding what differences from EPA's MDL procedures presented in Appendix D will actually be acceptable. This new flexibility may lead to more litigation.

Regarding improvements to this Section, a better correlation between the findings in Table 6-1 and the associated text would be useful. Within Table 6-1, it would also be useful to reference where in the TSD many of the statistics were derived. Also, the revised MDL procedures presented in Appendix D should be mentioned.

vi. **Prior to proposal of revised detection and quantitation concepts, should EPA evaluate other available data sets? Bearing in mind that in order to effectively assess various concepts, data sets must reflect measurements made below the detection limit, in the range of detection and quantitation limits, and in the normal measurement range of the method, are there any available data sets that you recommend EPA consider?**

During the 1980s numerous interlaboratory method evaluation studies were conducted by EPA's ORD group in Cincinnati, some of which may have looked at detection limits. Has EPA examined any of their historical work for pertinent MDL information? Also, as I recall, George Stanko of Shell presented a fairly large study challenging EPA's detection limits for volatile organics in water at EPA's annual Analytical Symposium in Norfolk, Virginia?

Has EPA petitioned large trade associations, such as the American Petroleum Institute (API), about detection and quantitation studies they may have sponsored?

Personally, I am not aware of any additional detection and quantitation limit data sets that may be of value to EPA.

vii. **Has EPA dealt with the interlaboratory *versus* intralaboratory issues appropriately and, if not what recommendations would you make for dealing with the issues more appropriately?**

The use of interlaboratory measurements is important for a general understanding of the laboratory communities' capabilities, but is not as relatable to the issues that EPA must consider in support of a permittee's CWA requirements. Intralaboratory

measurements are more practical. EPA's approach between inter- and intra- studies is balanced and reasonable.

viii. Can you recommend any improvements to the detection and quantitation procedures described in the TSD?

The MDL and ML concepts evaluated in Section 5.1.1 and 5.2.1, respectively, are shown in this evaluation to be technically sound and practical. The revised MDL procedure provided in Appendix D is streamlined and more intelligible than the previous version, although a reexamination of Step1 to aid chemists in the spiking level requirement may be warranted.

EPA's literature search was extensive, irregardless of my suggestions to examine some other sources. The detection and quantitation concepts I'm aware of have already been adequately "fleshed" out by EPA.

3. Specific comments for recommended changes or revisions needed to improve the clarity and scientific accuracy of the document.

Although the TSD is necessarily long and dense with information, it is well written and flows logically. I would not make any structural changes to the document. Since the TSD addresses fundamental quality assurance issues, I'm surprised that there is no acknowledgement or reference to EPA's Quality System. EPA may want to reexamine the TSD and update as appropiate to remain consistent with Agency directives.

A listing of acronyms would be useful.

Typos, grammar, etc.:

- Chapter 1 A detailed citation reference to the law suit and settlement agreement should be provided so that the reader can actually research the suit.
- Page 2-7 , text line 14 "most newer"?
- Chapter 3 If the 1997 EPA Method 1625 study has previously been published, it should be referenced.
- Page 3-7, text line 15 "give" should be "given".
- Section 3.2.1.4 First sentence incomplete.
- Section 3.2.1.4 A number of studies have been mentioned in the first paragraph. These should be referenced.
- Section 3.3.1 When discussing errors, should add systemic errors and blunders.
- Page 3-14, text line 11(first line of Section 3.3.1) Should add "analytical" before "measurement". Globally, the term measurement includes all sample collection and analysis activities.
- Page 5-3, text line 8 ">"3.05 should be "<"3.05 (Sentence beginning after "Step 4").
- Title of 5.2.1 "L" in limit should be capitalized.
- Page 6-1, text line 28 "be" should be inserted between "it" and "would".
- Reference Section Youden reference needs date (1975?)
- Appendix C, page C-11 PCB 1216 wrong. Should be PCB 1016?

4. **Any new information or data that could potentially improve the quality of the document.**

- Shumway et al., "Statistical Approaches to Estimating Mean Water Quality Concentration with Detection Limits," Environ.Sci.Technol. 36:3345-3353(2002).
- Yu et al., "Detection Limit of Isotope Dilution Mass Spectrometry," Analytical Chem. 74: 3887-3891(2002).
- A number of papers were published in the proceedings of the 224th American Chemical Society(ACS) National Meeting – Division of Environmental Chemistry, which was held in Boston in August 2002. Papers of interest for this exercise include: Currie, "Detection and Quantification Limits: Basic Concepts, International Harmonization, and Outstanding Issues"; Wade et al., "Method Detection Limits: Application to Organic Environmental Chemistry Data"; Rosecrance, "Recommended Guidelines for Generating Detection, Quantitation and Reporting Limits"; and Burrows, "Instrument Calibration in Environmental Analysis Issues and Proposals for Improvement".

Please don't hesitate to call me if you have any questions or require any clarifications about my opinions.

Sincerely,

GRADIENT CORPORATION

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